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SOCIAL SKILLS GROUP TRAINING FOR CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER

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Social skills group training for children and adolescents with autism spectrum disorder

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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I dedicate this work to my beloved daughter Linda and my husband Per.

ABSTRACT

The overall aim of this thesis was to examine the efficacy and effectiveness of social skills group training (SSGT) in children and adolescents with high functioning autism spectrum disorder (HFASD) and psychiatric comorbidity.

Prior to the trial, a systematic review was conducted on the effectiveness of randomized controlled trial (RCT) of SSGT. In addition, evaluation of two tools (Developmental Disabilities Children's Global Assessment Scale [DD-CGAS] and the OSU Autism Clinical Global Impression [CGI-S]) used in the trial, was performed. Sixteen vignettes of 8 clinical patients with HFASD and psychiatric comorbidity were rated by 16 clinicians. The trial was conducted based on the convergent mixed method approach (quantitative and qualitative). The quantitative, a multicenter pragmatic randomized control trial (PRCT) included a total of 296 children and adolescents with HFASD and psychiatric comorbidity aged 8 to 17 years. They were randomly assigned to an experimental (KONTAKT+ treatment as usual [TAU]) and a control group, TAU only. The qualitative study included 11 participants (6 high responders and 5 low responders) from the experimental group and their parents were interviewed and a qualitative responder analysis was performed.

The results showed a lack of information about recruitment, comorbidity, treatment providers, settings, and limited eligible population. The intraclass correlation coefficients (ICCs) for experienced clinicians were .75 for the DD-CGAS and .72 for the OSU Autism CGI. Among inexperienced clinicians, these ICCs were .58 and .59 respectively. The multicenter PRCT showed positive effects in experimental and control groups in social responsiveness skills. The experimental group showed a significant effect on social cognition, maintained after 3 months (B=-1.33, Z=-1.44, p=.02), but no effect according to blinded teacher ratings. Adolescents in the experimental group showed better results (B>-8.34, Z>-2.54 p< .001) for social responsiveness compared with the child group, particularly in social communication, but again not for blinded teacher ratings. Several secondary outcome measures identified improvements following SSGT. The qualitative study showed improvements in several areas of social skills. Even low-non-responders showed gains after treatment. Effectiveness studies are lacking that use RCTs for SSGT. Reliability is better for experienced vs less experienced clinicians for DD-CGAS and OSU Aut CGI. SSGT- KONTAKT can be successfully implemented in "real-world" clinical health care. Time effect for both KONTAKT+TAU and TAU are positive. A significant effect on social cognition in the experimental group was found. When compared to children, adolescents showed a greater positive effect in social communication, social motivation, and social cognition, whereas children had better effects in terms of everyday functioning, and symptom severity. Parents of children showed decreased stress, but no changes in perceived stress were identified among the children and adolescents after treatment. More efficacy and effectiveness studies on SSGT using convergent mixed methods (quantitative, qualitative) are needed before any robust conclusions can be drawn.

LIST OF SCIENTIFIC PAPERS

I. Jonsson U*, **Choque Olsson N***, Bölte S. Can findings from randomized controlled trials of social skills training in autism spectrum disorder be generalized? The neglected dimension of external validity. *Autism*. May 11 2015. [Epub ahead of print]. *Contributed equally

II. **Choque Olsson N**, Bölte S. Brief Report: "Quick and (not so) Dirty" Assessment of Change in Autism: Cross-Cultural Reliability of the Developmental Disabilities CGAS and the OSU Autism CGI. *Journal of autism and developmental disorders*. Jul 2014;44(7):1773-1778. [Epub ahead of print]

III. **Choque Olsson N**, Flygare O, Görling A, Råde A, Coco C, Chen Q, Lindsted K, Berggren S, Serlachius E, Tamimmies K, Kjellin L, Bölte S. Social skills group training, for children and adolescents with high functioning autism: A pragmatic multicenter and randomized controlled trial. (Manuscript)

IV. **Choque Olsson N**, Rautio D, Asztalos J, Stoetzer U, Bölte S. Social skills group training in high-functioning autism: A qualitative responder study. *Autism*. (In press).

SCIENTIFIC PAPERS NOT INCLUDED IN THE THESIS, BUT RELEVANT TO THE FIELD

I. **Choque Olsson N**, Karlsson A, Andersson S., Boström A, Ljungström M, Bölte S. Cross-cultural adaptation of social skills group training ("KONTAKT") for children and adolescents with high functioning autism spectrum disorder: A feasibility study. Scandinavian Journal of Child and Adolescent Psychiatry and Psychology. (In press).

II. **Choque Olsson N**, Tammimies K., Bölte S. Manualized social skills group training for children and adolescents with higher functioning autism spectrum disorder: Protocol of a naturalistic multicenter, randomized controlled trial. Translational Developmental Psychiatry, 3.29825. doi: http://dx.doi.org/10.3402/tdp.v3.29825

III. Neil L, **Choque Olsson N**, Pellicano E. The relationship between intolerance of uncertainty, sensory sensitivities, and anxiety in autistic and typically developing children. Journal of Autism and Developmental Disorders. (In press).

IV. Zander E, Willfors C, Berggren S, **Choque Olsson N**, Coco C, Elmund A, Moretti A. H, Holm A, Jifalt I, Kosieradzki R., Linder J, Nordin V, Olafsdottir K, Poltrago L, Bölte S. The objectivity of the Autism Diagnostic Observation Schedule (ADOS) in naturalistic clinical settings. European Child and Adolescent Psychiatry. Nov 19 2015 [Epub ahead of print].

CONTENTS

LIST OF ABBREVIATIONS

ABA	Applied Behavioral Analysis
ADDM	Autism and Developmental Disabilities Monitoring Network
ADHD	Attention Deficit/Hyperactivity Disorder
ADOS	Autism Diagnostic Observation Schedule
APA	American Psychiatric Association
APD	Antisocial Personality Disorder
AS	Asperger Syndrome
ASD	Autism Spectrum Disorder
BPD	Borderline Personality Disorder
CAHS	Child and Habilitation Services
CAMHS	Child and Adolescent Mental Health Services
CBI	Computer-based Interventions
CBT	Cognitive-Behavioral Therapy
CD	Conduct Disorder
CDC	US Centers for Disease Control and Prevention
CGAS	Children's Global Assessment Scale
CiS	Children in Stress
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
DANVA2	Diagnostic Analysis of Nonverbal Accuracy
DDC-GAS	Children's Global Assessment Scale for Developmental Disabilities
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition–Text Revision
EIBI	Early Intensive Behavioral Intervention
ES	Effect Size
FEFA	Frankfurt Test and Training of Facial Affect Recognition
HFASD	High Functioning Autism Spectrum Disorder
ICD-10	International Classification of Diseases and Related Health Problems, 10th Revision

IQ	Intelligence Quotient
K-SADS	Kiddie-Schedule of Affective Disorders and Schizophrenia
M	Mean
MeSH	Medical Subject Headings
OCD	Obsessive–Compulsive Disorder
OSU Aut CGI	OSU Autism Clinical Global Impression Scale
PDD	Pervasive Developmental Disorder
PDD-NOS	Pervasive Developmental Disorder-Not Otherwise Specified
PECS	Picture Exchange Communication System
PMI	Peer-mediated Interventions
PRCT	Pragmatic Randomized Controlled Trial
PRT	Pivotal Response Training
PSS	Perceived Stress Scale
RCT	Randomized Controlled Trial
SBU	Swedish Council for Medical Evaluation
SD	Standard deviation
SRS	Social Responsiveness Scale
SSGT	Social Skills Group Training
SSI	Social Skills Interventions
SSRS	Social Skills Rating System
TAU	Treatment As Usual
TEACCH	Treatment and Education of Autistic and Related Communication-Handicapped Children
VGI	Video-based Group Instruction
WISC-III	The Wechsler Intelligence Scale for Children-Third Edition
WISC-IV	The Wechsler Intelligence Scale for Children-Fourth Edition
WHO	World Health Organization

1 INTRODUCTION

1.1 AUTISM SPECTRUM DISORDER

Autism spectrum disorder (ASD) is an increasingly diagnosed early onset neurodevelopmental disorder characterized by persistent deficits in social communication and interaction, alongside repetitive, stereotypical behavior and restricted interests, according to the DSM-5 (APA, 2013) and upcoming International Classification of Diseases-11 (ICD) -11. The definition of ASD has undergone several changes since the diagnosis was established, but the impairment in social communication and interaction abilities as substantial criteria has not been changed since it was determined in the early 20th century[1]. ASD was included in the ICD-10 in 1992 (World Health Organization [WHO], 1992) and in DSM-IV in 1994 (APA, 1994). In 2000 the revised DSM-IV-TR (APA, 2000) described three subtypes of ASD: Autistic disorder, Asperger's disorder and Pervasive Developmental Disorders (PDD) not otherwise specified (NOS) which were defined under the umbrella term of Pervasive Developmental Disorders (PDD) together with Rett's disorder and childhood disintegrative disorder. The ASDs were characterized by impairment of reciprocal social interaction skills, communication skills, or the presence of stereotyped behaviors, interests, and activities. The latest revision of the DSM, DSM-5 (APA, 2013), adopted the umbrella term ASD without a definition of subtypes and reorganized the triad into dyad criteria: impairments in social communication and social interaction and restricted, repetitive behavior, interests or activities. Diagnostic reporting now includes specifiers that may enhance descriptive subtyping of the population, including specifiers for the presence or absence of intellectual impairment, language impairment, and catatonia as well as known medical, genetic, or environmental factors. Today, autism is seen as a dimensional construct and ASD is no longer considered a rare phenomenon, but a major health condition and societal challenge (APA, 2013).

[1] The first to describe symptoms of individuals with a condition similar to low-functioning ASD as patients with disintegrative disorders was Theodor Heller in 1908 (Mouridsen, 2003). In 1911, Eugen Bleuler described a group of patients who were especially withdrawn self-absorbed and distant from social situations by and he was the first to use the term "autism" (Stotz-Ingenlath, 2000). Furthermore, in 1926, Eva Ssucharenwa, published case observations of six boys with typical autism, described as having schizoid psychopathy which was a subtype of schizophrenia (Ssucharewa & Wolff, 1996). In 1943, Leo Kanner was the first to introduce the term "early infantile autism" to describe 11 children showing impairments in social interaction, language impairments, and difficulties in facing changes in the environment. He described this group as having a relatively rare developmental disorder (Kanner, 1943). A year later, in 1944, Hans Asperger identified ''autistic psychopathy' in childhood'' by describing four boys with high intelligence and difficulties in social communication (e g. lack of empathy, little ability to form friendships, one-sided conversation, some with special abilities or talents, "little professors") (Asperger, 1944) . In 1981, Lorna Wing revised the term "autistic psychopathy" and created two terms popular to this day, namely "Asperger syndrome" and "autism spectrum disorders" (Wing, 1981).

1.2 PREVALENCE

Numerous studies have tried to clarify the prevalence of ASD. The results have varied depending on the diagnostic criteria, age range, intelligence quotient (IQ) measurement, geographical area where the study was conducted, ascertainment method, and date of the study. In 2006, the US Center for Disease Control and Prevention (CDC) reported that about 1 in 110 8 year-old children in multiple areas of the United States had an ASD (CDC, 2006). The prevalence of ASD is estimated to have risen during the past decade and is now between ~1% (Baird et al., 2006; Gillberg, Cederlund, Lamberg, & Zeijlon, 2006) and ~2.6% (CDC, 2014; Idring et al., 2015; Kim et al., 2011). Possible reasons for this increase could be improved public awareness and services, broadening of diagnostic criteria used (e.g., the expanding criteria for ASD) (Matson & Shoemaker, 2009), the changes in definition (Volkmar et al., 2014), changing diagnoses of individuals previously diagnosed with different conditions i.e., "diagnostic substitution" (Shattuck, 2006), and probably an improvement in diagnostic tools that facilitate more accurate and earlier diagnosis, and better awareness and services. In terms of gender, all studies show a consistent male over-representation (2- 4 times more than females) (Idring et al., 2015; Newschaffer et al., 2007; Van Naarden Braun et al., 2015). Although the reason for the increase in ASD prevalence is unknown, the increasing number of children and adolescents diagnosed with ASD has led to an urgent need for evidence-based interventions targeting this population.

1.3 ASD AND PSYCHIATRIC COMORBIDITY

Intellectual disability (between 50% and 35%) and other medical conditions, such as epilepsy and language difficulties (Fombonne, 2009) are common comorbidities of an ASD diagnosis. Several studies have shown a high level of psychiatric comorbidities among individuals with ASD. Those with high-functioning autism disorder (HFASD) or with IQ > 70 can experience loneliness, bullying (Hebron & Humphrey, 2013; Mazurek, 2014) and high rates of co-existent psychiatric comorbidities, facing substantial challenges in adult life (Howlin & Moss, 2012). Simonoff et al. (2008) suggested that 70 % of children with ASD (12 to 14 years old) had at least one comorbid disorder and that 41% had two or more (Simonoff et al., 2008). According to that study the most common comorbid diagnoses were social anxiety disorder (29.2%), attention deficit/hyperactivity disorder (ADHD) (28.2%), and oppositional defiant disorder (28.1%). Other studies suggested a high prevalence of other psychiatric comorbidities such as mood disorders, fears, phobias, and obsessive–compulsive disorder (OCD) (Ghaziuddin, Ghaziuddin, & Greden, 2002; Jang et al., 2013; Matson & Cervantes, 2014; Mukaddes, Herguner, & Tanidir, 2010). A recent study showed that more than 70% of children with ASD have concurrent medical, developmental, or psychiatric comorbidities (Lai, Lombardo, & Baron-Cohen, 2014). That study also suggested that the high frequency of comorbidity could be the result of shared pathophysiology, shared symptom domains and associated mechanisms, or overlapping diagnostic criteria. Another factor in the increase in the prevalence of comorbidities in the last 5 years could be that multiple diagnoses were not

allowed according to DSM-IV-TR (APA, 2000) or the ICD-10 (WHO, 1992) . This restriction has been removed in the DSM-5 (APA, 2013). Studies regarding conditions comorbid to ASD are crucial in enhancing the awareness of the heterogeneity of ASD. The complexity of symptoms present in ASD needs to be considered in research and when delivering the interventions.

1.4 PARENT HEALTH

According to the literature, parents of children and adolescents with ASD are characterized by elevated rates of depression, anxiety, and addiction and an increased risk of divorce and sick leave compared to parents of typically developing children (Mugno, Ruta, D'Arrigo, & Mazzone, 2007; Schieve, Blumberg, Rice, Visser, & Boyle, 2007). ASD diagnosis in children causes additional stress for families and contributes to long-term societal costs (Schieve et al., 2012). Other studies suggest, however, that parents of children with autism and other disabilities are resilient and adopt effective coping strategies for daily problems (Tunali & Power, 2002) and that feelings of self-efficacy mediate levels of stress in mothers (Hastings & Brown, 2002). Several studies recommend inclusion of family measures of parental and family functioning in future studies of interventions to more fully understand the impact of interventions in a wider context (Kuhaneck, Madonna, Novak, & Pearson, 2015).

1.5 LIFETIME COSTS

Research estimates that the lifetime cost of caring for a child with an ASD ranges from $3.5 million to $5 million (ADDM., 2012). Based on these estimates, the United States is facing almost $90 billion annually in costs for ASDs. A recent study concluded that over the life of a child, expenses can go up to US $2.4 million per family, due to special education services by psychologists and speech therapists, and the added expenses of technology-based therapies (Buescher, Cidav, Knapp, & Mandell, 2014). These costs include research, insurance costs and non-covered expenses, educational spending, housing, transportation, employment, therapeutic services, and caregiver costs. These costs show the critical need for evidence-based intervention for this population and the need for studies regarding the cost–benefit relationship for certain interventions.

1.6 INTERVENTIONS IN ASD

ASD is considered non-curable (Bölte, 2014a); there is no treatment that cures its core symptoms. Several interventions, however, have been developed during the past 20 years (Hirvikoski et al., 2015) with the objective of reducing symptoms and preventing the onset of comorbid symptoms. Recent studies of cognitive-behavioral therapy (CBT) in children and adolescents with ASD with psychiatric comorbidities such as anxiety symptoms and behavior

problems have shown positive effects (Kreslins, Robertson, & Melville, 2015; White et al., 2013; Wood et al., 2009). A non-pharmacological intervention for co-existent comorbidities with empirical support for a positive effect is Applied Behavioral Analysis (ABA) (Reichow, Barton, Boyd, & Hume, 2012). The intervention is based on the learning principles of CBT. A widely disseminated comprehensive ABA program is Early Intensive Behavioral Intervention (EIBI) for young children, based on the work of Lovaas and colleagues (Lovaas et al., 1981). EIBI is intensive and highly individualized, with up to 40 hours per week of one-to-one direct teaching targeting preschool children. According to reviews EIBI is effective in young children (Howlin, Magiati, & Charman, 2009; Reichow, Barton, et al., 2012). However, proof of effectiveness of this intervention for school-aged children and adolescents with ASD is still limited. Other interventions such as Treatment and Education of Autistic and Related Communication-Handicapped Children (TEACCH) (Mesibov & Shea, 2011), and the Picture Exchange Communication System (PECS) (Agius & Vance, 2015; Charlop-Christy, Carpenter, Le, LeBlanc, & Kellet, 2002) have shown some promising evidence for positive effects or for some specific improvement in functional communication skills, for example initiating interactions (Ganz, Davis, Lund, Goodwyn, & Simpson, 2012). The efficacy of these interventions is, however, still unknown.

Numerous studies of interventions for individuals with ASD have shown low to moderate levels of evidence for a positive effect. Several systematic reviews (Kasari, Shire, Factor, & McCracken, 2014; Reichow & Volkmar, 2010; Rogers & Vismara, 2008) have critically evaluated these studies, showing that they vary in quality. This result points out the need for more and better quality studies if we are to reach robust conclusions. A review conducted by The Swedish Council on Health and Technology Assessment has found a strong ongoing need for intervention research in ASD (Swedish Council on Health Technology Assessment, 2013) as well as the need to enhance evidence-based treatment for patients with ASD in clinical health care (Hirvikoski et al., 2015). One non-pharmacological intervention with some evidence of a positive effect is social skills group training (SSGT) (Kasari et al., 2014; Reichow, Steiner, & Volkmar, 2012). In this thesis, we focused on SSGT for school aged children and adolescents with ASD.

1.7 SOCIAL SKILLS INTERVENTIONS

1.7.1 Definitions of social skills

Social skills are defined as complex constructs (Koenig, De Los Reyes, Cicchetti, Scahill, & Klin, 2009) that are associated with social competence. These terms are used when describing social skills interventions for individuals with ASD (Reichow, Steiner, et al., 2012). Several studies regarding social competence and social development in children with ASD consistently have indicated difficulties in key social skills. Gresham and Nagle (Gresham & Nagle, 1980) defined social skills as taught, learned, and performed behaviors. These behaviors are exhibited in different contexts and usually predict social outcomes for children

with and without ASD. Social competence is defined as the combination of a person's social skills and behaviors and how they are used in different contexts (Quinn, Kavale, Mathur, Rutherford, & Forness, 1999). Furthermore, social competence depends strongly on how those skills are evaluated and judged by others in the social environment (e g., parent, teachers, peers) (Gresham, Sugai, & Horner, 2001).

1.7.2 Cognitive theories

Multiple cognitive theories have been suggested to explain the causes of social difficulties in ASD. The numerous studies can be grouped based on three main theories. The first is deficits in theory of mind (Baron-Cohen, 1989; Begeer et al., 2011; Wing & Gould, 1979), which means that people with ASD lack the ability to take another person's perspective. The second theory is weak central coherence (Happe & Frith, 2006), a specific perceptual-cognitive style, suggesting that there is a limited ability to understand context or to "see the big picture" which is significant in social relations. The third theory is executive dysfunction (Prior et al., 1998; Rosenthal et al., 2013) which is associated with social communication, perseverative behavior, and difficulties switching flexibly between activities or adapting to different environments (Rosenthal et al., 2013). Despite the fact that each theory appears to have demonstrated value and applicability, it is likely that no single cause exists for social difficulties in ASD. Rather, these social difficulties are related to a complex set of multiple interacting factors (Pellicano, Maybery, Durkin, & Maley, 2006; Santangelo & Tsatsanis, 2005).

Difficulties in social skills and communication include: (1) lack of verbal and nonverbal communication abilities, including identifying faces and facial expressions (Bölte et al., 2006), lack of ability to take another person's perspective (Baron-Cohen, Tager-Flusberg, & Cohen, 2000; Begeer et al., 2011), and difficulty understanding the meaning of language (Prelock & Nelson, 2012); (2) lack of problem-solving abilities, such as regulating affect (Konstantareas & Stewart, 2006; McNally Keehn, Lincoln, Brown, & Chavira, 2013) and lack of insight and self-monitoring behavior (Attwood, 2007); and (3) poor peer relationships, social awareness, orientation, and social emotional reciprocity.

Numerous studies have focused on examining brain differences as a way to understand the mechanism underlying these difficulties; e.g., studies using Functional Magnetic resonance imaging to trace the mechanisms underlying a lack of interest in social stimuli, such as faces (Ashwin, Baron-Cohen, Wheelwright, O'Riordan, & Bullmore, 2007; Shah, Bird, & Cook, 2015) and avoidance of direct eye contact (Kliemann, Dziobek, Hatri, Steimke, & Heekeren, 2010). Literature on imaging and magnetoencephalography suggests that subjects with ASD exhibit reduced functional cortico- cortical connectivity (Alcauter et al., 2014; Khan et al., 2013). Furthermore, ASD is a highly heritable disorder associated with complex cognitive changes that lead to impairments in social interaction and language development (Klauck, 2006). A recent study suggested that mutations or deletions in the SHANK3 gene are associated with social and communicative skills in ASD (Philippe et al., 2015). Although,

numerous studies have addressed the social and communication difficulties in ASD, the mechanisms of these factors in more complex interactions between a person with ASD and their environment remain unknown.

Social demands become more complex with increasing age and an expected development towards independence, during which social difficulties might be exacerbated (Bohlander, Orlich, & Varley, 2012; Koenig et al., 2009; Rao, Beidel, & Murray, 2008; Reichow, Steiner, et al., 2012). Studies suggest that impairment in social interaction has a negative impact on the development of appropriate social competence in children and adolescents with ASD (Calder, 2013; Ratcliffe, Wong, Dossetor, & Hayes, 2015). Furthermore, other studies have shown that greater difficulties in social responsiveness are associated with poorer social skills, mental health difficulties (Ratcliffe et al., 2015), and experiencing loneliness and bullying (Braddock et al., 2015; Hebron & Humphrey, 2013; Zablotsky, Bradshaw, Anderson, & Law, 2014). Therefore, interventions that address social competency for this patient group appear critical in overcoming many of the negative and debilitating effects of these impairments. Although group-based interventions have often been implemented to enhance social skills and have yielded some evidence of positive effect (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012), the effectiveness or the generalizability of these interventions has been neglected (Jonsson, Choque Olsson, & Bölte, 2015; Kaat & Lecavalier, 2014; Kasari et al., 2014; Reichow, Steiner, et al., 2012; Williams, Keonig, & Scahill, 2007).

1.7.3 Types of social skills training

Although multiple strategies have been proposed to promote social skills in children and adolescents with ASD, social skills interventions (SSI) have attracted the most attention in the past 20 years among researchers and clinicians (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012; Williams et al., 2007). SSI is an umbrella term used for group training with the objective of increasing social skills in individuals with ASD (Bohlander et al., 2012), including instruction and reinforcement techniques such as social problem-solving scripting procedures, prompting procedures, and self-monitoring priming to increase the frequency and quality of social behaviors of individuals with ASD (Antshel et al., 2011; Pugliese & White, 2014) in specific settings. It is based on the concept that learning social skills requires specific training and more opportunities to practice social skills over time and in everyday life (Rogers & Vismara, 2008). The most frequently used SSGT programs are as follows:

1.7.3.1 Peer-mediated interventions

Peer-mediated interventions (PMI) involves peers in the social skills training program, which is traditionally used with preschool-aged children within the regular classroom (Bohlander et al., 2012), but the model also is used even in adolescents and adults (Watkins et al., 2015). Typically developing peers are taught how to interact with children with autism to encourage the development of their social skills. In this model a peer may be taught, for example, how to be a good friend, and to continue to communicate with a peer with ASD even if the child

with ASD does not respond initially. Children with ASD participate in general education classrooms alongside typically developing children. The program is delivered in many ways; including in class-wide interventions, training sessions, groups, tutoring, integrated play (Watkins et al., 2015), or peer-mediated, theater-based intervention (Corbett et al., 2015; McFadden, Kamps, & Heitzman-Powell, 2014). A recent review on PMI suggested that it is a promising treatment for increasing social interaction for children, adolescents, and young adults with ASD in inclusive settings, with positive generalization and maintenance. Nevertheless, this method has some limitations, because without a rigorous intervention, typically developing peer children tend to play with other typically developing peers rather than with children with ASD (Bohlander et al., 2012). There is evidence that it is important to carefully consider the participant characteristics and the type of social deficit when choosing the optimal configuration of PMI strategies (Watkins et al., 2015).

1.7.3.2 Video modeling

Video modeling is used to teach social skills to children and adolescents with ASD using minimal adult support and interaction (Bellini & Peters, 2008; Hume, Loftin, & Lantz, 2009). Video modeling is rooted in Bandura's Social Learning Theory, stating that human behavior is primarily learned by observing and modeling others, which modeled behavior that could be presented in vivo or recorded (Corbett & Abdulla, 2005). In vivo modeling consists of the therapist demonstrating the behavior to the child, and having them imitate or "model" the appropriate behavior. A meta-analysis suggests the effectiveness of video modeling and video self-modeling interventions (Bellini & Peters, 2008). A recent study showed that video-based group instruction (VGI) is useful for teaching novel social behavior and shows support for its use for some adolescents with ASD and intellectual disabilities (Plavnick, Kaid, & MacFarland, 2015).

1.7.3.3 Social stories

Social stories are short, individualized, and written in first person with the objective of teaching social skills or behaviors to individuals with ASD. The method was introduced by Carol Gray in 1993 and involves parents or teachers (Gray & GarandJoy, 1993). The short story is about a skill, activity, or event and lets the child know what, when and where the situation or event will happen, along with the expected behavior or response from the child with ASD. A study has shown that social stories are useful for children with ASD and problem behavior (Pane, Sidener, Vladescu, & Nirgudkar, 2015). There is some evidence of effectiveness for social stories when used as part of a more comprehensive social skills program (Scattone, Tingstrom, & Wilczynski, 2006; Thiemann & Goldstein, 2001).

1.7.3.4 Pivotal response training

Pivotal response training (PRT) (Koegel, Bradshaw, Ashbaugh, & Koegel, 2014) is an intervention program based on the principles of applied behavioral analysis. PRT uses a natural environment and targets pivotal behaviors, which are behaviors that lead to widespread changes in other behaviors and that facilitate the transfer of skills to multiple

settings and collateral improvements in non-targeted behaviors. PRT targets four pivotal areas: responsiveness to multiple cues, initiation, motivation, and self-management. The efficacy of PRT has been supported by numerous studies (Humphries, 2003; Stahmer, 1995; Symon, 2005). A recent review indicated support for PRT as an effective, efficacious and naturalistic intervention to improve the communication skills and social functioning of children with ASD (Cadogan & McCrimmon, 2015).

1.7.3.5 Computer-based intervention

Computer-based interventions (CBIs) have been implemented to teach children with delays in theory of mind development to acquire social cognitive skills. Programs, techniques, and classes have demonstrated positive outcomes in regard to theory of mind, perspective-taking skills, and recognition of face emotions. Various virtual environments, including CBI, have been used effectively to teach social skills to individuals with ASD (Lahiri, Bekele, Dohrmann, Warren, & Sarkar, 2015; Mitchell, Parsons, & Leonard, 2007; Parsons, Mitchell, & Leonard, 2004). Bölte et al., (2002) found support for the usefulness of the CBI program for teaching the detection of facial affect in youths with ASD (Bölte et al., 2002). Another study showed that older subjects with ASD seem to have better skills than younger subjects with ASD after the intervention using the Frankfurt Test and Training of Facial Affect Recognition (FEFA)(Kuusikko et al., 2009). Two studies have examined the effectiveness of Mind Reading, using an interactive computer software program (Golan & Baron-Cohen, 2006; Golan, Baron-Cohen, Hill, & Golan, 2006). They found that adults with ASD showed marked improvement in recognizing emotions in pictures and voices presented similarly as within the computer program, but showed less improvement when presented with photographs of an individual's eyes only or film clips not presented in the computer program format. A recent study showed a significant effect on emotion encoding and decoding skills and social skills at post treatment and at 5-week follow-up (Thomeer et al., 2015). A review of CBI in ASD suggests that this method is promising when trying to improve the social and emotional skills of individuals with ASD but that it could be more effective if combined with tutoring and face-to-face instructions (Ramdoss et al., 2012).

1.8 SOCIAL SKILLS GROUP TRAINING

Social skills group training (SSGT) is one of the most commonly implemented interventions for school-aged children and adolescents with ASD. The traditional group consists of approximately 4 or 5 children with ASD, with the training being delivered by a therapist or teacher. The participants learn social skills in interaction with other peers. Session topics might include greeting others, being friendly, joining or initiating play with others, reading nonverbal cues, and starting and maintaining conversations.

1.8.1 Efficacy and effectiveness

Despite the need for evidence-based interventions aimed at children and adolescents with ASD, few interventions have been rigorously evaluated (Rao et al., 2008; Williams et al., 2007). SSGT is one of the most commonly implemented intervention methods used for school-aged children and adolescents with ASD during the past 20 years. A review from 2007 that included 14 studies on SSGT reported several methodological problems such as small samples, inadequate measure of social skills, and the need for improvements. The authors suggested phases of research on evidence-based interventions as follows. The first phase needs focus on method development or "technique refinement" such as modification of existing techniques by using case studies. The second development phase could focus on the development of manualized interventions, and in the third phase, a manualized intervention could be evaluated using randomized controlled trials (RCTs). Finally, a fourth phase would be multicenter RCT studies to measure the effectiveness of SSGT (Williams et al., 2007). Another review from 2008, based on 10 studies, identified several limitations such as a lack of control group, lack of a common definition of specific social skills in subgroups of ASD, small sample sizes, insufficient power, and lack of generalization of treatment effects (Rao et al., 2008). In 2012, a review of the efficacy of SSGT confirmed previous findings related to methodological flaws such as the absence of a treatment manual, lack of control groups, small samples, undefined inclusion and exclusion criteria, use of unstandardized outcome measures, and a failure to report effect sizes (Reichow, Steiner, et al., 2012). The authors identified five RCTs with some quality (with a combined total of 196 participants) and concluded that there is some evidence that SSGT improves overall social competence (effect size [ES] =.47, 95% confidence interval [CI] .16 to .78, p=.003) and friendship quality (ES= .41, 95% CI .02 to .81, p =.04) (Reichow, Steiner, et al., 2012), but more studies are needed to allow robust conclusions. The authors recommended adequate power to detect clinically important effects. In 2013, a review conducted in Sweden by the Swedish Council for Medical Evaluation (SBU) considered only one study on SSGT (Beaumont & Sofronoff, 2008) with enough scientific quality (Swedish Council on Health Technology Assessment, 2013). The authors concluded that studies on SSGT showed insufficient quality and relevance because of the lack of a randomization process and an active control. They pointed out an ongoing strong need for intervention research in ASD. Some improvements have been made in relation to these methodological problems regarding the efficacy of SSGT (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012). Nevertheless, the effectiveness or generalizability of SSGT has still not been systematically reviewed and the generalizability of the RCT studies remains neglected.

1.8.2 Explorative and pragmatic RCT

RCT studies are considered the "gold standard" for treatment research or treatment evaluation (Schulz, Altman, & Moher, 2010; Thorpe et al., 2009), but RCT studies also have shown some limitations, particularly in regard to implementation of the study results in community-based health care interventions. There are two types of RCTs: (1) the exploratory RCT, which tests the efficacy of an intervention and tries to answer the question of whether an

intervention can have a beneficial effect, and (2) the pragmatic RCT (PRCT), which measures effectiveness and the degree of beneficial effect of the intervention program conducted in "real-world" clinical practice and involving current patients (Godwin et al., 2003). The exploratory RCT is conducted in an ideal situation, for instance, several intervention programs have been developed and tested within university based or specialized research contexts with high staff-to-participant ratios, high levels of intensity, highly trained clinicians, and rigorous adherence to clearly defined treatment strategies. In contrast, the PRCT is conducted in regular settings, and it is not uncommon that the research is integrated into the routines of care services and takes in to account the symptom complexity of patients (Rothwell, 2006; Ware & Hamel, 2011) (Table 1).

Table 1. Differences between studies on efficacy and effectiveness of RCT studies

Events in a typical RCT/intern validity	Events in the PRCT/intern and extern validity
Participants are recruited from specialist centers, or by advertising.	Participants are mainly recruited from a regular clinic care.
Participants with comorbid medical or psychiatric disorders are excluded.	Participants with comorbid disorders are included.
Participants are carefully selected to generate homogeneous diagnostic groups according to DSM and ICD.	Participants are current patients and they are included even with heterogeneity by using clinical assessment in accordance with DSM or ICD.
Use randomization.	Use randomization.
Patients are given detailed information (which may be over-inclusive) for informed consent	Patients are provided detailed information.
An active control group is used for comparison with the experimental group.	A treatment as usual is used for comparison with the experimental group.
The intervention is delivered in research settings with optimal conditions	The intervention is delivered in regular and real world clinical care.
Intervention providers are educated and trained to deliver only the treatment used in the study.	Intervention providers are educated and trained to deliver the treatment, but they mostly consider the law of patient care in a community-based clinic
Participants are followed at frequent intervals.	The intervention is based on a curriculum by using manualized programs and following the current routines of the regular clinics.
Patient and clinician are blind to treatment group.	Both (usually) are aware of the treatment the patient is given.

While the explanatory RCT seeks to maximize internal validity by assuring rigorous control of all variables with the objective of minimizing bias, the PRCT seeks a balance between external validity (generalizability of the results) and internal validity (reliability or accuracy of the results) (Godwin et al., 2003). It compares a new intervention to treatment as usual (TAU) which allows for generalizability of the PRCTs' findings and thus can be translated

into practice and policy (Maclure, 2009; Thorpe et al., 2009; Ware & Hamel, 2011). To the author knowledge, no PRCT studies on SSGT have been conducted. For more information on the differences between RCT study and PRCT studies see Table 1.

1.8.3 Internal and external validity

As mentioned above, to achieve a maximized internal validity in trials, researchers commonly use RCT studies to avoid systematic bias, e.g., decreasing selection bias by using a homogeneous population and excluding those who have a complex symptomatology, using blinded observers, and blind data analysis (Harrington, Cartwright, & Stein, 2002; Rothwell, 2006; Schulz et al., 2010). Consequently, these studies, despite good results, become less useful in regular settings because of difficulties implementing the program in more complex conditions (Lutz, 2003). On the other hand, external validity is maximized by having few exclusion criteria and allowing flexibility in interpretation of the intervention and in management decisions (Maclure, 2009). An attempt to achieve methodological purity can lead to clinically meaningless results, and attempting to achieve full generalizability can result in invalid and unreliable results. Achieving a balanced tension between these two extremes is crucial (Godwin et al., 2003; Rothwell, 2006; Thorpe et al., 2009).

Some efforts have been made to study the effectiveness of SSGT, e.g., in adults (Howlin & Yates, 1999), but no efficacy analysis has been performed. A review of behavior-based interventions found a positive effect, but included only a RCTs with high quality (Shire & Kasari, 2014). Another study examining an intervention based on theory of mind showed promising effects (Adibsereshki, Nesayan, Asadi Gandomani, & Karimlou, 2015), but there were several limitations regarding generalizability. Several studies have focused on parent intervention (Stadnick, Stahmer, & Brookman-Frazee, 2015) but few studies on SSGT have focused on both internal and external validity.

1.8.4 Convergent mixed methods research (quantitative and qualitative study)

As mentioned above, how to best evaluate the effect of an intervention has been under discussion for the last 20 years. Although quantitative studies are used to address effect studies of treatments, qualitative research is used to explore why or how a phenomenon occurs or to describe the nature of an individual's experiences participating in a certain treatment (Brown, 2001). These study methods have been used separately, and few studies have applied both quantitative and qualitative approaches to evaluating intervention effects. Studies based on mixed research methods are needed for an innovative approach to addressing complex issues in real health care (Creswell, Klassen, Plano Clark, & Smith, 2011; Dattilio, Edwards, & Fishman, 2010; Fetters, Curry, & Creswell, 2013). Qualitative research elucidates the results of quantitative studies (Bölte, 2014b; O'Cathain, Thomas, Drabble, Rudolph, & Hewison, 2013). Despite an increase in the number of RCT studies with improved methodological rigor (Kaat & Lecavalier, 2014), several important areas of SSGT research still have not garnered attention, hampering a better understanding of SSGT usability

and feasibility. One example is the scarcity of involvement of individuals with ASD in the research (Pellicano, Dinsmore, & Charman, 2014): No studies have considered the view of individuals with ASD and their experiences participating in a SSGT. To the author's knowledge, no studies on SSGT in ASD based on a mixed method approach have been undertaken to date.

1.9 METHODOLOGICAL CHALLENGES

1.9.1 Sample size

A common methodological problem in treatment effect studies is small sample sizes. According to a recent review, few RCT studies on SSGT had more than 20 participants (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012). Larger samples are needed to allow for better control over subject variability, thereby increasing both internal and external validity.

1.9.2 Inclusion and exclusion criteria

There has been some improvement in the description of inclusion criteria in RCT studies, but information about exclusion criteria is still insufficiently reported (McMahon, Lerner, & Britton, 2013; Williams et al., 2007). Despite evidence of a high prevalence of secondary psychiatric comorbidities among individuals with ASD, as mentioned above, the inclusion and exclusion of comorbidity in the eligible populations is unknown. A better description of the study's eligible population is crucial to define internal validity and also generalizability, which can be helpful for identifying those for whom a treatment might be effective (Howlin & Yates, 1999; Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012).

1.9.3 Recruitment process

The recruitment process is essential information to facilitate the replication of the study as well as the generalizability. Information about the allocation and assessment processes is scarce (e. g., if a study was announced, if there were other factors in the exclusion of participants such as the participants' awareness of the diagnosis, motivation, and practical impairments), which hampers study participation (McMahon, Lerner, et al., 2013; Swedish Council on Health Technology Assessment, 2013; Williams et al., 2007). More studies in the field are needed to increase the reporting of the recruitment process of prior RCT studies and the generalizability of these results.

1.9.4 Treatment providers

Information about the characteristics of the treatment provider is crucial for trial replicability and generalizability. Reports about the treatment provider's education, supervision (duration/time), and training of the therapist who delivered the treatment remains insufficient. The therapist's experience, profession, education, and treatment adherence have an impact on treatment outcome, and the reporting of this information facilitates replicability in other

settings (Garland, Haine-Schlagel, Accurso, Baker-Ericzen, & Brookman-Frazee, 2012; Rothwell, 2006).

1.9.5 Settings and number of settings in the study

The setting in which the treatment is delivered is crucial to the generalizability of the study (Rothwell, 2006). Despite some improvement in the reporting of the settings, during the last few years, the majority of studies have been conducted in university-based specialty treatment clinics. Few studies were implemented in community-based settings or ‘‘real-world’’ clinical settings.

1.9.6 Manualized programs

Treatment manuals are necessary for conducting and replicating clinical trials (Rao et al., 2008; Smith & Iadarola, 2015). Recent reviews on SSGT have revealed some improvements in using manualized programs and in the reporting of duration and frequency, intensity, and treatment fidelity of the program (Kaat & Lecavalier, 2014; McMahon, Lerner, et al., 2013). Although the majority of RCT studies use a manualized program, information is lacking about whether these programs have been evaluated during a prior feasibility study (Rao et al., 2008; Williams et al., 2007). In addition, the content of these programs varies, hampering the analysis of which program content gives a positive effect; for instance, some interventions focused only on initiation, responding to social interactions, friendship, and nonverbal or verbal communication (McMahon, Lerner, et al., 2013).

1.9.7 Outcome

Reviews showed that primary and secondary outcome measures in RCT studies on SSGT are insufficiently reported. On the other hand, there is no consensus on which outcome measures should be used. The most frequent outcome measures for SSGT effect are the Social Responsiveness Scale (SRS), Social Skills Rating System (SSRS), and Diagnostic Analysis of Nonverbal Accuracy (DANVA2) (Reichow, Steiner, et al., 2012). Changes regarding every day functioning, which are important according to the DSM-5 (APA, 2013), or symptom severity are, however, not sufficiently studied. Only two studies have reported change in these areas (Koenig et al., 2010; White et al., 2013). Most reports showing significant effects of social skills do not cite effect sizes, and few studies have followed up treatment outcomes over time or the effect of the groups*time effect (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012). It is challenging for RCT researchers to carry out follow-up measurements because of drop-outs and to follow the treatment effect over time.

1.9.8 Blinded assessment

Perhaps the most difficult methodological issue for clinical interventions in a naturalistic setting is the double-blind method, which is a standard in drug trials (Harrington et al., 2002).

Despite the need for blinded observation with an objective minimization of the risk of bias in trials (Reichow, Steiner, et al., 2012), few studies to date on SSGT have involved blinded raters.

2 AIMS OF THIS DOCTORAL PROJECT

The overall objective of this thesis was to examine the efficacy and effectiveness of SSGT in children and adolescents with HFASD and psychiatric comorbidity. The specific aims of each study in this thesis are presented below.

2.1 STUDY I

The objective of study I was to conduct a systematic review of RCT studies on SSGT for children and adolescents with HFASD, focusing on external validity. The purpose was to identify areas of underreported external validity, and to subsequently develop a checklist to be used as support in our multicenter PRCT of study III. This checklist can be recommended for future research to increase generalizability.

2.2 STUDY II

The objective of study II was to investigate the clinical utility and inter-rater reliability of the Swedish version of the Children's Global Assessment Scale for Developmental Disabilities (DD-CGAS) and the OSU Autism Clinical Global Impression scale (OSU Autism CGI) used in RCTs.

2.3 STUDY III

The objective of study III was to examine the efficacy and effectiveness of SSGT-KONTAKT in children and adolescents with HFASD with psychiatric comorbidity compared to TAU as delivered in several naturalistic settings.

2.4 STUDY IV

To achieve a deeper understanding of the treatment effect of SSGT-KONTAKT as a supplement to quantitative PRCT, Study IV was qualitative, aimed at examining participant and parent experiences among those who participated in KONTAKT training after the treatment was conducted.

3 METHODS

3.1 GENERAL CONSIDERATIONS

As presented in the Introduction, several methodological flaws limit prior studies on the efficacy of SSGT. As a consequence, the effectiveness or generalizability of these programs in real-world health care is still unknown. In addition to the main objective described in chapter 2, the purpose of the current thesis was to overcome methodological shortcomings of these previous studies. For this purpose, we used a convergent mixed (quantitative and qualitative) study design. The quantitative study was a multicenter PRCT with a large sample size (N=296). It included participants from a regular setting with secondary psychiatric comorbidity with an intervention relying on previously evaluated manual-based intervention. The study was characterized by well-defined inclusion and exclusion criteria and used computerized randomization, psychometrically evaluated outcome measures, and clinicians as treatment providers with education and supervision. Finally, the study was conducted in outpatient clinics within the regular healthcare system. The study was registered in Clinical Trials.gov Identifier: NCT0185434633 and followed the study protocol (Choque Olsson, Tammimies, & Bölte, 2015). The qualitative study followed the guidelines presented by Braun and Clarke, 2006 (Braun & Clarke, 2006) and based on the quantitative study. The trial followed the study protocol (Choque Olsson et al., 2015) and the recommendations presented in CONSORT (Schulz et al., 2010) (Appendix 1) and the "Checklist for reporting external validity information in RCT studies" (Jonsson et al., 2015) (Appendices 2).

To describe the study implementation and structure the thesis has been divided into two parts (Table 2):

(1) Studies prior to the trial:

- Study I aimed to review the effectiveness and generalizability of prior RCT studies on SSGT by systematic reviews focused on external validity, and
- Study II aimed to evaluate two of the tools used in the PRCT of Study III.

(2) Studies related to the trial: aimed to evaluate the efficacy and effectiveness of SSGT-KONTAKT using a convergent mixed method design, including

- Study III, a quantitative, multicenter PRCT study, and
- Study IV, a qualitative study (Table 2).

Table 2. Structure of the included studies

Structure	Study	Type of study	Design
Studies prior to the trial	**I**	Exploratory study of RCTs focused on SSGT	Systematic review
	II	Quantitative Instrument evaluation	Experimental cohort study
Studies related to the trial using a convergent mixed method design	**III**	Quantitative Treatment evaluation	Experimental, multicenter PRCT, prospective study [NCT01854346]
	IV	Qualitative	Convergent qualitative study: a responder, non-responder analysis

3.2 STUDY SUBJECTS

3.2.1 STUDY I

A total of 15 RCT studies on SSGI were included in the review (Table 3). Participants (N=553) were children and adolescents with a diagnosis of ASD, autism, Asperger syndrome (AS), or PDD-NOS as diagnosed using the DSM-IV (APA, 1994), DSM-IV-TR (APA, 2000) or ICD-10 criteria (WO, 1992) ages 7 to 18 years; and with a minimum verbal IQ level (60–85) using the Wechsler Intelligence Scale (WISC-III or WISC-IV) (Wechsler, 1991, 2004).

3.2.2 STUDY II

Sixteen clinical vignettes of 8 (3 girls and 5 boys) patients with HFASD and psychiatric comorbidities were included in the study (Table 3). The children and adolescents were current outpatients from Child and Adolescent Mental Health Services (CAMHS) in Stockholm. The vignettes described patients aged 8 to 16 years who fulfilled the DSM-5 (APA, 2013), and Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000), and ICD-10 (WHO, 1992) criteria for ASD such as autism, AS or PDD-NOS. The described patients had borderline to high IQs (75–120). Each vignette comprised extensive clinical descriptions of the individual's situation, symptomatology, and treatment for two points in time: one for clinical referral and the other for discharge.

Table 3. Study participant characteristics

Study	Participants	Inclusion criteria	Exclusion criteria	Comorbidity
II	8 clinical patients described in the vignettes	ASD according to DSM-IV-TR and with IQ ≥70	IQ ≥70; ASD without comorbidity	ADHD, Anxiety disorder, depression, OCD according to ICD-10
III	N=296 participants: n=150 KONTAKT +TAU n= 146 TAU	ASD, according to DSM-IV-TR, ICD-10, ADOS and an IQ > 70 according to WISC-IV/ WAIS III	Self-injury, CD, APD, BPD, or any form of schizophrenia or related psychotic disorder	ADHD, anxiety disorder or depression according to DSM-IV, ICD 10 and by using K-SADS
IV	N=22 participants n= 11 children and adolescents who completed KONTAKT intervention n=11 parents	ASD according to DSM-IV-TR, ICD-10; ADOS, and an IQ ≥70 according to WISC-IV/WAIS III Parents of participants who were included in the experimental group	Self-injury, CD, APD, BPD, or any form of schizophrenia or related psychotic disorder -	ADHD, anxiety disorder or depression, clinical diagnosis by using K-SADS -

Notes: ADHD: Attention Deficit/Hyperactivity Disorder; ADOS: Autism Diagnostic Observation Schedule; APD: antisocial personality disorder; ASD: Autism Spectrum Disorder; BPD: Borderline Personality Disorder; CD: Conduct disorder; DSM-IV-TR: Diagnostic and Statistical, 4th Edition. Manual of Mental Disorders-Text Revision; HFASD: Higher-functioning Autism Spectrum Disorder; ICD-10: International statistical classification of diseases, 10th Revision; IQ: Intelligence Quotient; K-SADS: Kiddie-Schedule of Affective Disorders and Schizophrenia; OCD: obsessive-compulsive disorder; TAU: treatment as usual; WISC-III: Wechsler Intelligence Scale for Children-Third Edition; WISC-IV: The Wechsler Intelligence Scale for Children-Fourth Edition.

3.2.3 STUDY III

A total of 366 participants, all children and adolescents with HFASD aged between 8 and 17 years old, were enrolled, and 296 were included (Table 3). The eligible criteria were: HFASD as defined by ICD-10 (WHO, 1992) (F84.0, F84.1, F84.5, or F84.9) plus meeting the cut-off for ASD (social interaction) on the ADOS (Lord et al., 2000; Lord, Rutter, & Le Couteur, 1994); IQ ≥70 according to WISC-IV/WAIS III (Wechsler, 1991, 2004), and secondary psychiatric diagnosis as defined by ICD-10 diagnoses (ADHD, F90.0 or F90.8; anxiety disorder (F40, F41 or F43); or depression, F32 or F33 by using the Kiddie-Schedule of Affective Disorders and Schizophrenia (Jarbin & Ivarsson, 2010)). Exclusion criteria were the presence of clinically diagnosed self-injury, conduct disorder (F91), hyperkinetic

conduct disorder, F90.1, antisocial personality disorder (F60.2), borderline personality disorder (F60.3), or any form of schizophrenia or related psychotic disorder (F20- F29).

All included participants were clinically diagnosed with HFASD as defined by the criteria described above. Of 366 participants assessed for eligibility, 70 were excluded and 296 were included in the trial. The participants were stratified into two age groups, children (n=172) and adolescents (n=124). They were randomized to the experimental group SSGT-KONTAKT+TAU or the control, TAU group, as follows: SSGT-KONTAKT+TAU, n=150 (n=83 children, n=67 adolescents), and TAU, n= 146 (n=89 children, n=57 adolescents). The study groups (children and adolescents) were largely comparable in terms of age, gender, IQ, ASD diagnoses, comorbidity, and pharmacological treatment. There were no differences in age, marital status, education, or occupation among the parents of the experimental and control groups.

3.2.4 STUDY IV

In total, 22 individuals were included and interviewed in this study (Table 3): 11children and adolescents aged 8-17 years old with a primary diagnosis of HFASD, and one parent of each child or adolescent participant. The child and adolescent participants were previously diagnosed by experienced, multidisciplinary assessment teams consisting of child psychiatrists, psychologists, pediatricians, social workers, and occupational therapists within CAMHS in Stockholm using ICD-10 criteria (WHO, 1992) and regional clinical guidelines for the assessment and treatment of ASD. Eleven children and adolescents with ASD and psychiatric comorbidity who participated in SSGT KONTAKT were selected from the PRCT [NCT01854346], and their parents were included in the study. Six high-responders and five low-non-responders were selected based on their results on the primary outcome (the SRS).

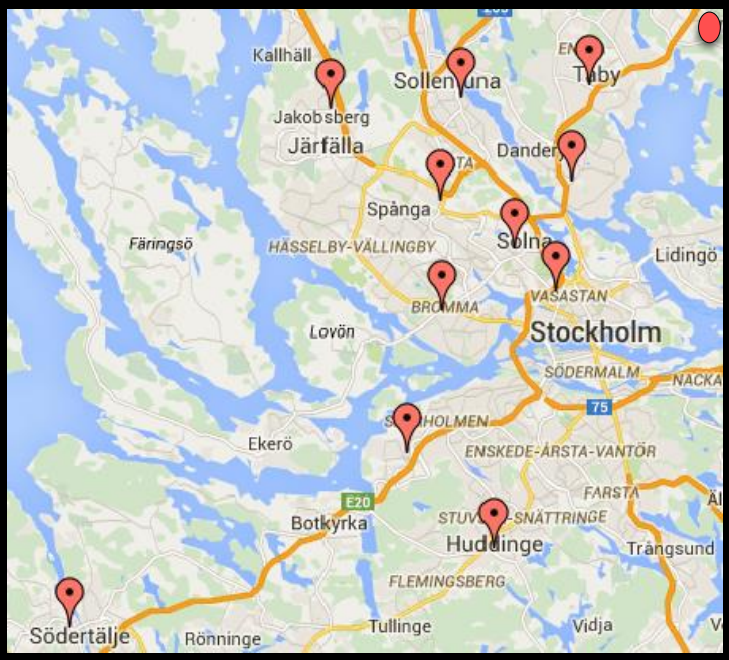
3.3 SETTINGS

All participants in studies III and IV were recruited from 11 clinics at Child and Adolescent Mental Health Services in Stockholm [CAMHS] (Brommaplan, KIND, Danderyd, Jakobsberg, Mellanvård Nordost, Mellanvård Sydväst, Solna, Sollentuna, Södertälje, Skärholmen and Täby) (Figure 1). The majority of participants in the PRCT in study III were recruited and trained at 11 CAMHS in Stockholm (92.2 %). The remaining participants were recruited at PRIMA-barn Järva (3.7 %) and from Child and Adolescents Habilitation Services (3 %).

Figure 1. Clinical settings

Child and Adolescent Mental Health Services (CAMHS) in Stockholm

- BUP* Brommaplan
- BUP Danderyd
- BUP Jakobsberg
- BUP KIND
- BUP Mellanvården NO
- BUP Mellanvården SV
- BUP Sollentuna (2012-2013)
- BUP Solna
- BUP Skärholmen
- BUP Södertälje (2012-2014)
- BUP Täby



PRIMA-barn Järva, Stockholm (2013-2014)

Child and Adolescents Habilitation Services (CAHS) in Örebro (2014-2015)

(* BUP: Swedish acronym for Child and Adolescent Mental Health Services)

The CAMHS in Stockholm is the largest child and adolescent mental health care service provider in Sweden, with about 1,000 employees, a total of 25,000 patients treated annually, and 170,000 annual visits at 17 outpatient clinics. There are four outpatient clinics offering more intensive treatments, two inpatient clinics, and five specialized units providing highly specific care. In accordance with local health care policies, CAMHS typically serves complex cases of ASD (ASD with psychiatric comorbidity), and patients with ASD without

comorbidity are served by Child and Adolescents Habilitation Services (CAHS) in Örebro in Stockholm. This structural definition has been the major reason that the participants included in the studies in this thesis have one or several psychiatric comorbidities in addition to the ASD diagnosis.

PRIMA-Järva is a private child and adolescent psychiatric clinic in Stockholm. The staff includes 18 employees (specialist doctors, nurses, psychologists, student psychologists, social workers, and special pedagogic assistants).

The CAHS in Örebro consist of 87 employees: physicians, psychologists, counselors, special educators, speech therapists, occupational therapists, physiotherapists, and medical care administrators. The team provides habilitation to children and adolescents from the age of 7 with ASD diagnosis and normal intelligence.

3.4 THE MANUALIZED PROGRAM KONTAKT

The program KONTAKT is a structured SSGT for children and adolescents with HFASD. The program was used in both studies III and IV. KONTAKT was developed in Germany (Poustka, Bölte, & Herbrecht, 2007) and adapted to Swedish conditions (Bölte & Choque Olsson, 2011). The program was evaluated in two pilot studies, the first conducted in Germany (Herbrecht et al., 2009) and the second in Sweden (Choque Olsson et al.). KONTAKT is based on cognitive behavioral principles by using positive reinforcement and homework assignments for generalizability and theories of social cognition that are adapted to individuals with ASD. The program content teaches participants to initiate social overtures, conversation skills, the understanding of social rules and relationships, identification and interpretation of verbal and nonverbal social signals, managing conflicts, and coping strategies to improve self-confidence. The treatment includes conveyance of common social rules and norms as well as problem-solving strategies, group discussions, social play, and emotion processing, training role-play, group activities, homework assignments, and individual behavioral analysis. Participants are assigned to groups for either children (8-12 years) or adolescents (13-17 years). The treatment frequency is weekly, with 1-hour training for children and 1.5 hours for adolescents. There are two treatment forms: the short treatment (12 sessions, 3 months) and long treatment (24 sessions, 6 months). In this thesis, the short treatment was used. The groups consist of four to six participants and two trainers. Parent involvement in the training as well as teacher cooperation is also embedded in the KONTAKT program.

3.5 TREATMENT AS USUAL

The control group of the Study III received no SSGT-KONTAKT after randomization. They were asked to continue their regular health-care with unrestricted access to services.

Medical journals were searched for pharmacological treatment, psychological treatment, general counselling, and other intervention.

3.6 OUTCOME MEASURES

To increase the scope of the impact of SSGT, we used primary and several secondary outcome measures with multi-informants such as parent, teacher, clinician, and participant ratings in both studies III and IV. The outcome measures covered social skills adaptive behavior in children and adolescents with HFASD, and perceived stress in both participants and parents measured at three time points: pretreatment, post treatment, and at 3 months of follow-up.

3.6.1 Social Responsiveness Scale

The SRS (Constantino & Gruber, 2005), rated by parents and by school teachers blinded to treatment group, was used as the primary outcome measure. The SRS assesses participant's social skills with a 65-item dimensional rating scale from 0 (never true) to 3 (almost always true). It is appropriate for use with children and adolescents from 4 to 18 years of age. The psychometric properties of the SRS have previously been tested in a study involving over 1900 children aged 4–15 years and have yielded good reliability and good validity. Specifically, previous research has found a test–retest reliability coefficient of 0.88 for the total scaled score (Constantino, Przybeck, Friesen, & Todd, 2000) and a high external validity and a test-retest reliability of 0.91-0.97 (Bölte, Poustka, & Constantino, 2008). The quantitative nature of the tool makes it useful for measuring the response to interventions over time, and previous research has shown that SRS is sensitive to changes in social functioning among children with ASD (Constantino & Gruber, 2005; Laugeson, Frankel, Gantman, Dillon, & Mogil, 2012; Wood et al., 2009). In the current study, the coefficient alpha for the total score was acceptable at α =.84.

3.6.2 The Adaptive Behavior Assessment System II

The Adaptive Behavior Assessment System II (ABAS-II) (Harrison & Oakland, 2003), based on parents and blinded school-teacher ratings, was used to measure adaptive functioning and indexes the generalization of change outside the clinical environment. The ABAS II includes communication, social, community use, functional academics, school/home living, health and safety, leisure, self-care and self-direction, and four composite scores are derived from the sum of the scaled scores: general adaptive composite, conceptual, social, and practical. A study showed the ABAS-II is useful for measuring adaptive impairments, in HFASD (Kenworthy, Case, Harms, Martin, & Wallace, 2010). The Swedish version of ABAS-II was adapted and validated in 2007 (Tideman, 2008). The internal consistency (reliability) for parents (N=30) was α =.98 and was α =.98 for teachers (N=233).

To use well-evaluated outcome measures in the multicenter PRCT (study III), we examined the clinical utility and inter-rater reliability of the DD-CGAS (as described in 3.5.3) and OSU Aut CGI-S (as described in 3.5.4).

3.6.3 The Developmental Disabilities Modification of the Children's Global Assessment scale

The DD-CGAS (Wagner et al., 2007) is an instrument that clinicians use to rate a patient's global everyday functioning. The scale ranges from 1, which indicates an extremely and consistently reduced ability, to 100, which indicates extremely good functioning in all areas of life (e.g., at home, school, and in social relations). Scores below 70 on the DD-CGAS indicate clinically relevant atypical functioning. It is a modified version of the standard CGAS to better fit children and adolescents with ASD. The scale has been translated and validated for Swedish conditions (Choque Olsson & Bölte, 2014) and evaluated in study II (Appendix 3). The study design and results are described in study II.

3.6.4 The Autism Clinical Global Impression-Severity scale

The OSU Aut CGI-S (OSU Research Unit on Pediatric Psychopharmacology, 2005) is a clinician-based rating scale aimed at estimating the global impression of symptom severity. The global clinical impression is rated on 7 point scales of ASD and other symptom severity, with 7 indicating extremely severe symptomatology, and 1 indicating no sign of clinical symptomatology. The CGI scale is widely used as an outcome measure in a number of intervention studies in psychiatry as well as a tool in pharmacological trials (Siegel et al., 2014). The original CGI scale (Guy, 1976) was modified and standardized in individuals with ASD (OSU Research Unit on Pediatric Psychopharmacology, 2005) and adapted to Swedish conditions (Choque Olsson & Bölte, 2014) (Appendix 4). The study design and results are described in study II.

3.6.5 Perceived Stress Scale

Parental stress was measured by using the Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983), a 14-item instrument measuring stress related to everyday life. The PSS is a global assessment of an individual's perception of psychological stress during the past week. Each item is rated on a 5-point scale, and scores are calculated after reverse keying positive items and totaling the scores. Possible total scores range from 0 to 52, with a higher score indicating greater stress, although this effect is nonlinear. The PSS is not a diagnostic instrument, and no predetermined cut-off points delineate different levels of perceived stress. The Swedish translation has demonstrated good internal consistency (Cronbach's $\alpha = .82$) (Eskin & Parr, 1996) and has shown satisfactory psychometric properties.

3.6.6 Children in Stress

Participant stress was measured by using the Children in Stress (CiS) (Osika, Friberg, & Wahrborg, 2007), a 21-item instrument measuring stress in children, using descriptions of

physical and emotional symptoms of stress. It has demonstrated good internal consistency (Cronbach's α =.86) and shows strong correlations (r =.53-.66) with Beck Youth Inventories (Beck, Beck, Jolly, & Jolly, 2005).

3.7 PROCEDURE

3.7.1 STUDY I

Two reviewers independently screened the titles and abstracts of all the citations identified by using Medical Subject Headings (MeSH) and relevant text word terms. Five databases (Medline, PubMed, PsycInfo, Cinahl and ERIC) were searched up to December 19, 2014. Studies of potential relevance for SSGI were screened a second time by two reviewers. If deemed necessary at this stage, the article was obtained in full text, and two reviewers independently assessed it for inclusion. Any disagreements were resolved by discussions with a third reviewer. Reference lists and systematic reviews were screened for additional studies of relevance.

3.7.2 STUDY II

Prior to the study, the English versions of DD-CGAS and OSU Aut CGI-S were translated and adapted to Swedish and piloted by three therapists. Furthermore, eight vignettes comprising extensive clinical descriptions of patients with ASD with psychiatric comorbidities and their clinical symptomatology and treatment were used. The vignettes hade two time points, and each vignette was rated by 16 therapists (8 at referral and 8 at discharge) by using DD-CGAS and the severity scale of the OSU Autism CGI. The clinicians had varying professional backgrounds, clinical experience, and professions 11 psychologists, 3 social workers and 2 nurses). Thirteen were women and 3 were male, all between ages 31 and 62 years (mean [M]=42 years). Eleven (69 %) had masters and five (31 %) bachelor degrees. Their clinical experience ranged from 1 to 40 years (M=7.8 years), and they were divided into two groups: n=8 experienced (> 2 years clinical experience with ASD) and n=8 inexperienced (< 2 years clinical experience). The clinicians were recruited to participate as group leaders in PRCT (study III). Furthermore, these two evaluated tools were used in the multicenter PRCT in study III.

3.7.3 STUDY III

Prior to the multicenter PRCT, two tools were evaluated as described in study II. There were also supplementary workbooks for group leaders, participants, and parents, developed as a curriculum of the Swedish version of KONTAKT. The author of the thesis recruited the therapists and child and adolescent clinics by presentations and information about the upcoming study. In total, 13 clinical settings and 50 regular therapists were recruited during the study period (August 2012 to September 2015).

Recruitment

Once clinics and therapists were recruited, the study was advertised on the homepage and in pamphlets at the CAMHS in Stockholm, Karolinska Institutet and interested organizations in Sweden. The majority of participants (80%) were recruited through referrals from each study clinic. Those who applied through self-referrals were contacted by the research coordinator for a short telephone screening interview and to give general information about the treatment and study protocol. When the first screening was positive, the participants were directed to an available clinic based on age and location. An intake interview was conducted before the applicant's eligibility was confirmed. The interview also focused on giving more detailed information about the treatment and study protocol. Written informed consent was obtained from both participants and parents. The staff at each clinic checked the medical records of their applicants to verify the presence of required diagnoses and gathered available results from WISC(Wechsler, 1991, 2004) and ADOS (Lord et al., 1994).

Diagnostic assessments

All enrolled participants had been previously diagnosed by experienced, multidisciplinary assessment teams consisting of child psychiatrists, psychologists, pediatricians, social workers and occupational therapists within clinics at CAMHS in Stockholm by using ICD-10 (WHO, 1992) criteria and clinical guidelines in Sweden for the assessment and treatment of ASD and other psychiatric conditions. All participants' documented diagnostic clinical assessments were checked in their medical records to confirm the diagnostic criteria. Finally, the medical record was scanned for results from WISC (Wechsler, 1991, 2004) and ADOS (Lord et al., 2000; Lord et al., 1994). In some cases when the test results of WISC and/or ADOS were more than 5 years old or were missing, a supplementary assessment was performed by clinical psychologists at the BUP-KIND, one of the child and adolescent clinics.

Randomization

Randomization was performed by a senior researcher using computer-generated random numbers [http://www.random.org] based on the stratification into age groups of children and adolescents. Participants in each group were randomly assigned to the experimental or control group by using block randomization in a 1:1 ratio.

Treatment provider

Throughout the trial, a total of 50 clinicians (psychologists, social worker, nurses, speech therapists, vocational therapists, and special pedagogics participated as group leaders) with experience working with ASD received education and supervision. All providers of training received 2 days of intensive classroom and applied practice training, as well as 4 hours of monthly supervision and consultation by telephone or e-mail during the study. Those clinicians who had led two KONTAKT groups and attended at least eight supervising sessions and recorded a session received the KONTAKT group leader certification. During the supervising sessions, video-recorded sections of treatment were shown and discussed to

ensure treatment fidelity. The KONTAKT education and supervision were implemented at the Center of Neurodevelopmental Disorders at Karolinska Institutet by a senior psychotherapist who worked with the Swedish adaptation of the KONTAKT program and the main supervisor. All therapists were required to demonstrate 90% or greater fidelity in implementing the treatment protocol during applied practice exercises, by following the therapist book.

Assessments for treatment response

Assessments for treatment response were performed at three time points: T1, pretreatment; T2, post treatment; and T3, at 3 months of follow-up after the end of intervention. The first assessment (T1) was implemented after inclusion of the child and the decision of parents and child/adolescents to participate. The assessment comprised questionnaires for participants, parents, and teachers following an interview with the participants and their parents. The second assessment (T2) was performed after completed treatment, including questionnaires for parents, child/adolescents, and teachers, and an interview with the child or adolescent with their parents. Furthermore, at 3 month assessment after the treatment, a follow-up (T3) with all instruments included at T2 for parents and participants was implemented. Assessments for treatment response for the TAU groups were performed within the same time frame.

3.7.4 STUDY IV

Participants were interviewed using a structured interview guide regarding their experience of participating in SSGT KONTAKT as well as with the structure and content of the program. An interview guide was developed before and piloted for feasibility in five children and adolescents with ASD to explore participant experiences and opinions on SSGT. The interview guide contained questions about their perceived changes in social and other skills and their views regarding the structure and content of KONTAKT. The interviewers were two clinical psychologists with a minimum of 5 years of clinical experience working with children and adolescents with ASD, assisted by a psychology student. The average duration of the interviews was 30 minutes for the participating children and adolescents and 45 minutes for their parents. To avoid bias, the interviewers were blind to the participant's group membership, and they had not been previously involved in the participant's SSGT.

3.8 DATA ANALYSIS

3.8.1 STUDY I

Three researchers conducted the data analysis. Identification criteria were clustered into five overarching themes related to external validity: eligible population, included population, context, treatment provider, intervention, and outcome. For each coded item,

the coding was summarized across all included studies. In a narrative synthesis, we summarized the extracted information for the whole body of included studies.

3.8.2 STUDY II

Two-way random intra class correlations (ICCs) (with 95 % CI) in SPSS 20 were calculated to determine interrater reliability for all case vignettes and all possible pairs of raters for both the DD-CGAS and the OSU Autism CGI-S, as well as separately for experienced and less experienced clinicians. The ICC classification by Landis and Koch (1977) was used to interpret the findings, with ICC≤.20 indicating slight, .21–.40 fair, .41–.60 moderate, .61–.80 substantial, and .81–1.00 (almost) perfect agreement (Landis & Koch, 1977). In addition to ICCs, Pearson correlation between DD-CGAS and the OSU Autism CGI ratings was computed. In terms of construct validity, we expected a high negative correlation between the DD-CGAS (with increasing values indicating higher adaptive functional skills), and the OSU Autism CGI-S (with increasing values indicating higher symptom severity).

3.8.3 STUDY III

The main analysis of the data for the included 296 participants was conducted according to intention-to-treat principles (Armijo-Olivo, Warren, & Magee, 2009). Because missing data were distributed randomly, mixed-effect modeling (Gueorguieva & Krystal, 2004; Lane, 2008) was used to examine time*treatment effect. The model was specified by using time (pre-, post and follow-up), group (KONTAKT+TAU vs. TAU), and the time*group interaction as fixed effects, with a random intercept for each stratified age group. The same model was used to investigate changes in all secondary outcome measures for continuous data. The Wilcoxon signed ranks test was used for the ordinal data. In addition, effect sizes of primary outcome measures between groups were calculated using Cohen's *d* (Cohen J., 1988).

3.8.4 STUDY IV

The analysis of study IV was performed using a thematic analysis (Braun & Clarke, 2006). The interviews were audio recorded and transcribed verbatim and then coded to condense interview material into consistent emergent themes, aided by NVivo 10. The thematic analysis was conducted as follows:

1) Familiarization with the transcribed material by the three researchers.
2) Generation of nodes by two independent raters through review of the verbal data using NVivo 10, based on the pooled participant and parent statements [after controlling the statements and findings, no substantial differences between participant and parent interview data were found]. The extracted nodes were reviewed by the third researcher and discussed with the research team in cases of uncertainty.
3) Identification of the themes by grouping of the initial nodes into themes (e. g., "improved social skills").

4) Revalidation of themes against initial verbal data [derived themes that were not indicated consistently enough in the raw material were deleted; possible similar themes were classified into larger groups].
5) Finalizing definition and labels of themes.
6) Comparison of the structure and composition of emerging themes regarding the experiences of SSGT of high-responders versus low-responders for both the children/adolescents and their parents.

3.9 ETHICAL CONSIDERATIONS

All studies were approved by the Regional Ethical Review Board in Stockholm, Sweden. Written informed consent was obtained from all participants in studies II, III, and IV. Studies II and III were prospective experimental studies, and study IV was qualitative; participants were thus informed about the research, and the randomization procedure that determined how the participant would be assigned to the experimental KONTAKT+TAU or control group, TAU. These who were assigned to the TAU were offered the treatment after completing the study. Furthermore, patients were recruited from a regular child and adolescent clinic in Stockholm that offers mental health care in accordance with National Board of Health and Welfare (Socialstyrelsen). These studies were implemented in accordance with Swedish Data Protection Authority (Datainspektionen) regulations.

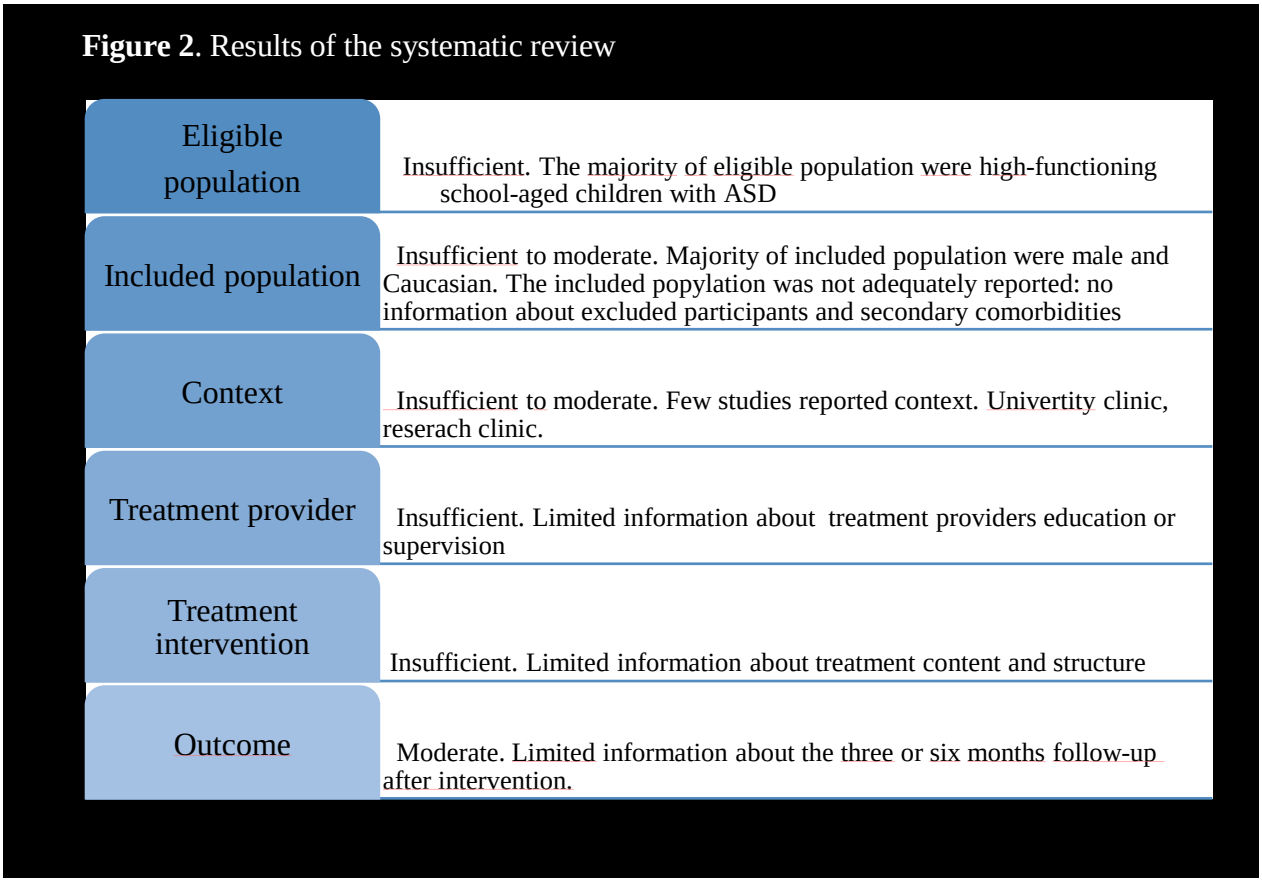
4 RESULTS

This chapter presents the results of the studies. The subsequent chapter reports these findings within the context.

4.1 STUDY I. EXTERNAL VALIDITY OF RCT STUDIES ON SOCIAL SKILLS GROUP INTERVENTIONS

Initially, we identified 8515 records, and after removing the duplicates and screening according to the inclusion criteria, there were 217 assessed for eligibility. A total of 199 were excluded for different reasons, and 15 eligible RCTs were included in the synthesis (Baghdadli et al., 2013; Beaumont & Sofronoff, 2008; Begeer et al., 2011; DeRosier, Swick, Davis, McMillen, & Matthews, 2011; Frankel et al., 2010; Koenig et al., 2010; Koning, Magill-Evans, Volden, & Dick, 2013; Laugeson, Frankel, Mogil, & Dillon, 2009; Lerner & Mikami, 2012; Lopata et al., 2010; Schohl et al., 2014; Solomon, Goodlin-Jones, & Anders, 2004; Thomeer et al., 2012; White et al., 2013; Yoo et al., 2014). The systematic review showed that the eligible population for the trials was limited to high-functioning school-aged children with ASD, and the included population was predominantly male and Caucasian. There was lack of information about the recruitment, treatment providers and settings. It was not evident from the trials to what extent acquired social skills were enacted in everyday life and maintained over time (Figure 2).

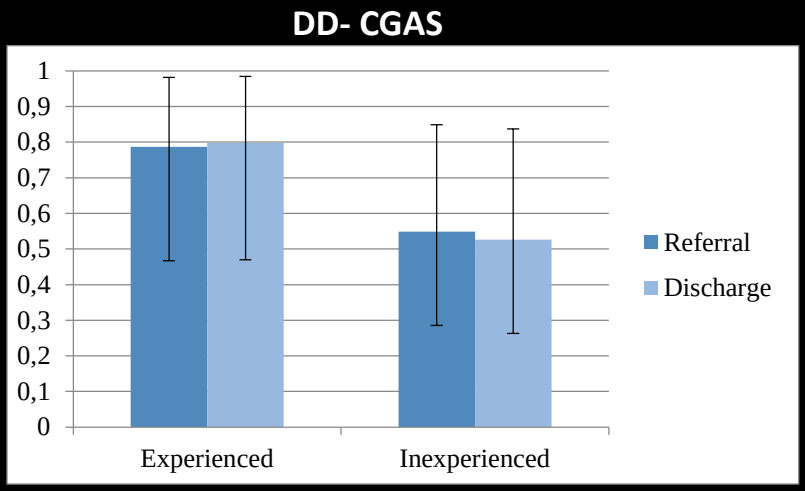
Figure 2. Results of the systematic review



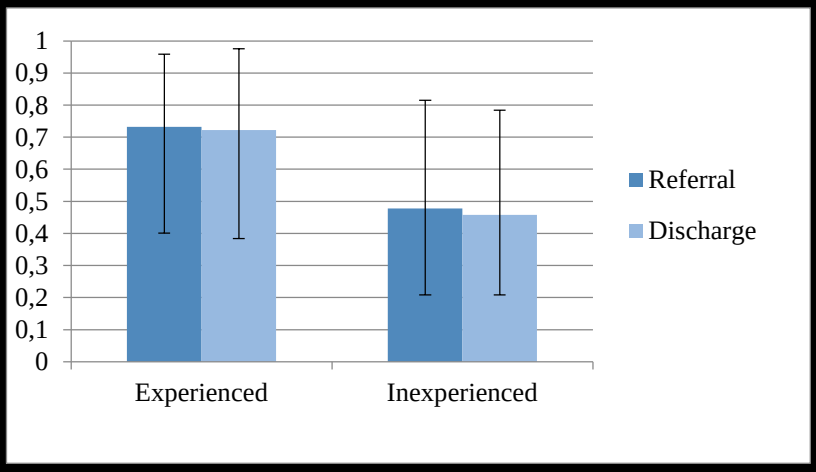
4.2 STUDY II. VALIDATION OF DD-CGAS AND OSU AUTISM CGI-S

The results showed that the ICC for all raters (experienced and inexperienced) was .63 for the DD-CGAS and .60 for the OSU Autism OSU Aut CGI-S. On the DD-CGAS, ICC was .75 for more experienced clinicians and .58 for less experienced ones. On the OSU Aut CGI-S, the ICC was .72 for experienced and .59 for inexperienced clinicians. The Pearson correlation between DD CGAS and OSU Aut CGI-S was .86 at referral and -.82 at discharge (Figure 3).

Figure 3. ICC results for DD-CGAS and OSU Aut CGI-S for experienced and inexperienced raters at referral and at discharge



a. On the DD-CGAS, ICC =.75 (ICC.78 referral, .79 discharge) for experienced, and .58 (ICC=.54 referral, .53 discharge) for inexperienced clinicians.



b. On the OSU Aut CGI-S, ICC = .72 (ICC.73 referral, .72 discharge) for experienced and .59 (ICC=.48 referral, .46 discharge) for inexperienced clinicians.

4.3 STUDY III. EFFICACY AND EFFECTIVENESS OF SSGT-KONTAKT FOR CHILDREN AND ADOLESCENTS WITH HFASD

Both groups: children and adolescents together, KONTAKT+TAU vs TAU

Social responsiveness: Parent ratings on SRS total-scores in KONTAKT+TAU and TAU showed significant effects over time in both groups: B=-6.07, Z=- 4.27, p≤ .001 at post treatment and B=-6.81, Z=-4.44, p≤ .001 at follow-up. There were significant effects in SRS subscales including social cognition (B=-1.33, Z=-1.44, p=.02) at follow-up. Blinded teacher ratings on SRS subscales showed no significant effects. Between the KONTAKT+TAU and TAU analyses, there was a difference in SRS subscales for autistic mannerisms at post-treatment and follow-up (post: *d* = -0.30; follow-up: *d* =-.22) and social motivation (*d* =-.34) at follow-up.

Adaptive abilities: Significant effects of SSGT-KONTAKT+TAU and TAU were seen over time on ABAS-II in the general adaptive composite at both post treatment (B=3.73, Z=2.47, p=.01) and follow-up (B=3.25, Z=2.03, p=.04) as well as in the subscales for adaptive social skills at post treatment (B=3.01, Z=2.30, p=.02) and adaptive social relation at follow-up (B=1.56, Z=1.92, p=.05). No significant effect was seen on blind teacher ratings. In regard to ABAS II subscales, there was a significant effect on functional academics at post treatment and follow-u (B>2.83, Z>2.34, p=.02).
Global and everyday functioning: According to clinician ratings on the DD-CGAS, there was a significant effect in the total scores at follow-up (B>2.43, Z>2.90, p≤ .001).
Symptom severity: the results of clinician ratings on the OSU Aut CGI-S showed significant differences at pre-post and pre-follow-up both groups, but the KONTAKT+TAU showed the greater effect (Z=<-4.9, p≤.001).
Parents perceived stress: There was significant in total scores at follow-up (B= -3.58, Z= -3.39, p≤ .001).
Participants perceived stress: no significant effect was found.

Age-group analysis: (children and adolescent group)*time interaction, KONTAKT+TAU vs TAU

Social responsiveness: A significant effect was seen for adolescents according to parent ratings on SRS total-scores at both post training (B=-8.34, Z=-2.54, p=.01) and follow-up (B=-8.60, Z=-2.46, p=.01). Regarding the subscale of SRS, there was a significant effect in the adolescent group in social communication at both post-training (B=-2.92, Z=-2.08, p=.04) and follow-up (B=-3.89, Z=-2.59, p=.01); in social motivation at post-training (B= -1.90, Z= -2.26, p= .02) and follow-up (B=-2.41, Z= -2.69, p=.01), in social cognition at follow-up (B=-1.82, Z=-2.04, p=.0) and in autistic mannerisms at post training (B=-1.58, Z= -2.11, p=.04). There were no significant effects in the child group. Blinded teacher ratings showed similar results (Figure 4).

Adaptive abilities: There was a significant effect in parent ratings on the ABAS-II among the adolescents for the general adaptive composite score at post treatment (B=5.97, Z=2.90, p≤.001), as well as on several subscales. Blinded teacher ratings showed a significant effect in the adolescent group for free time at follow-up (B=3.74, Z=2.15, p=.03), as well as in the child group in functional academics at post treatment (B=3.22, Z=2.25, p=.03).

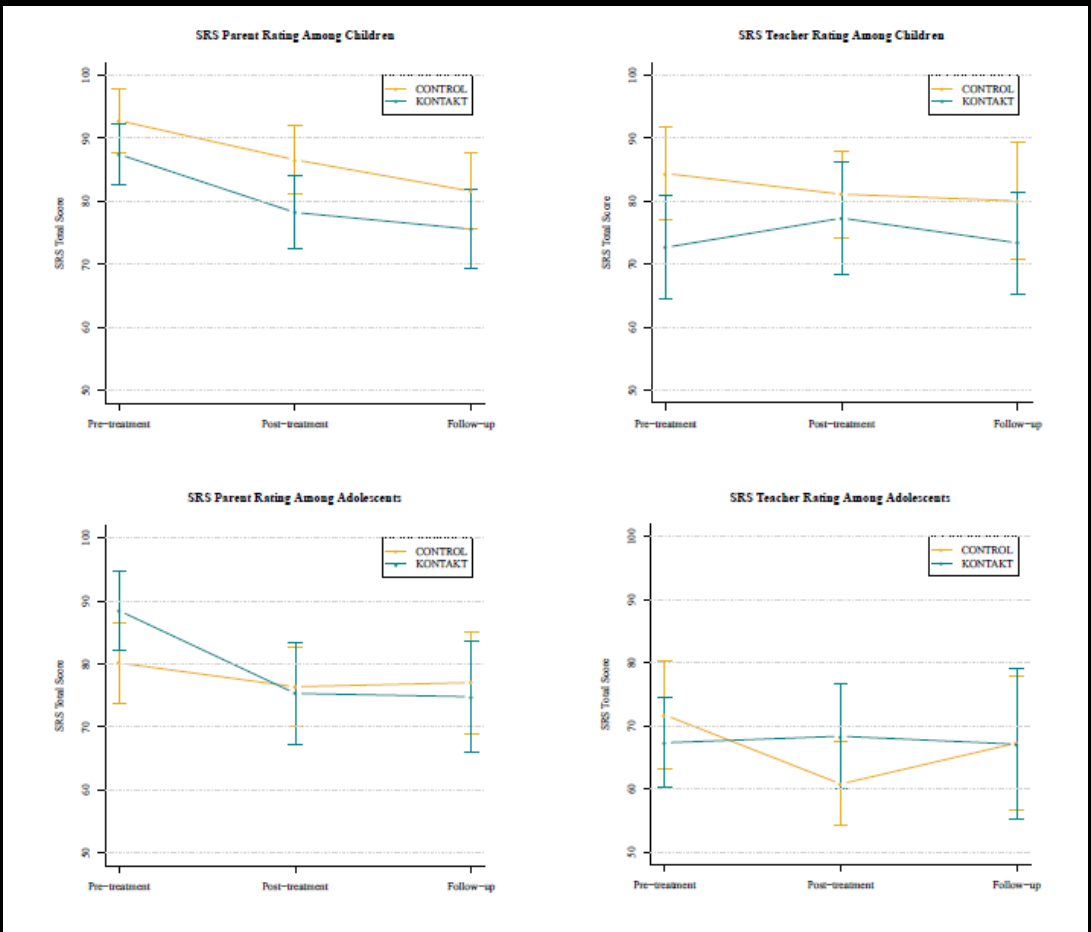
Global and everyday functioning: There was a significant effect in the child group at post treatment (B=2.32, Z=2.97, p=≤.001) and follow-up (B=3.4.0, Z=3.50, p=≤.001) while there was no significant effect in the adolescent group (Figure 4).

Parents perceived stress: The results showed a significant effect in total scores in the child group at follow-up (B=-4.59, Z=-3.21, p<.001).

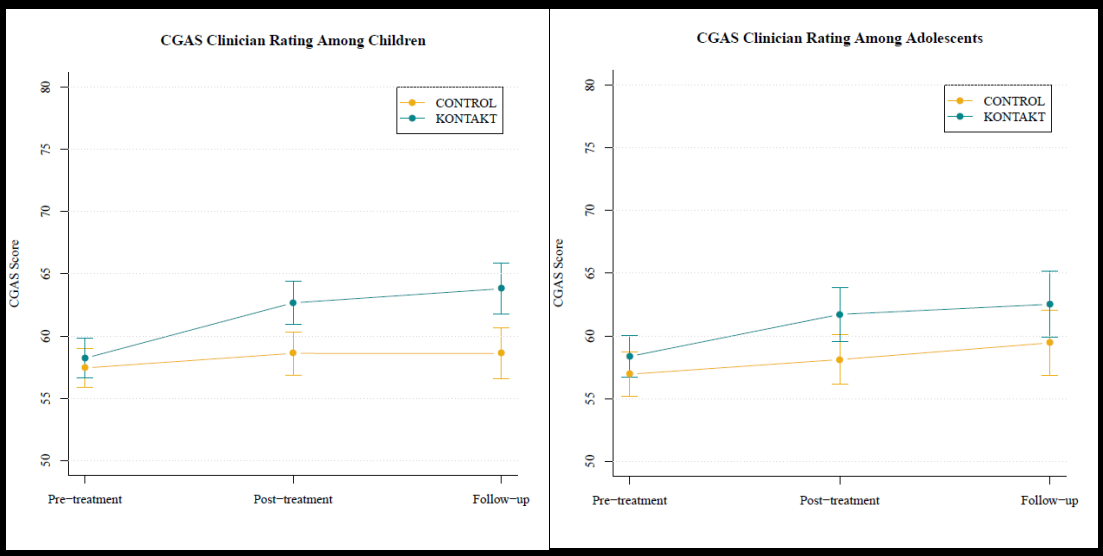
Participants perceived stress: There was no significant effect in either child or adolescent groups.

Figure 4: Results: social responsiveness and global functioning

a) Parent and blinded teacher ratings on Social Responsiveness Scale (SRS) total-cores for both children and adolescents



b) Clinician ratings on DD-CGAS, global functioning among children and adolescents

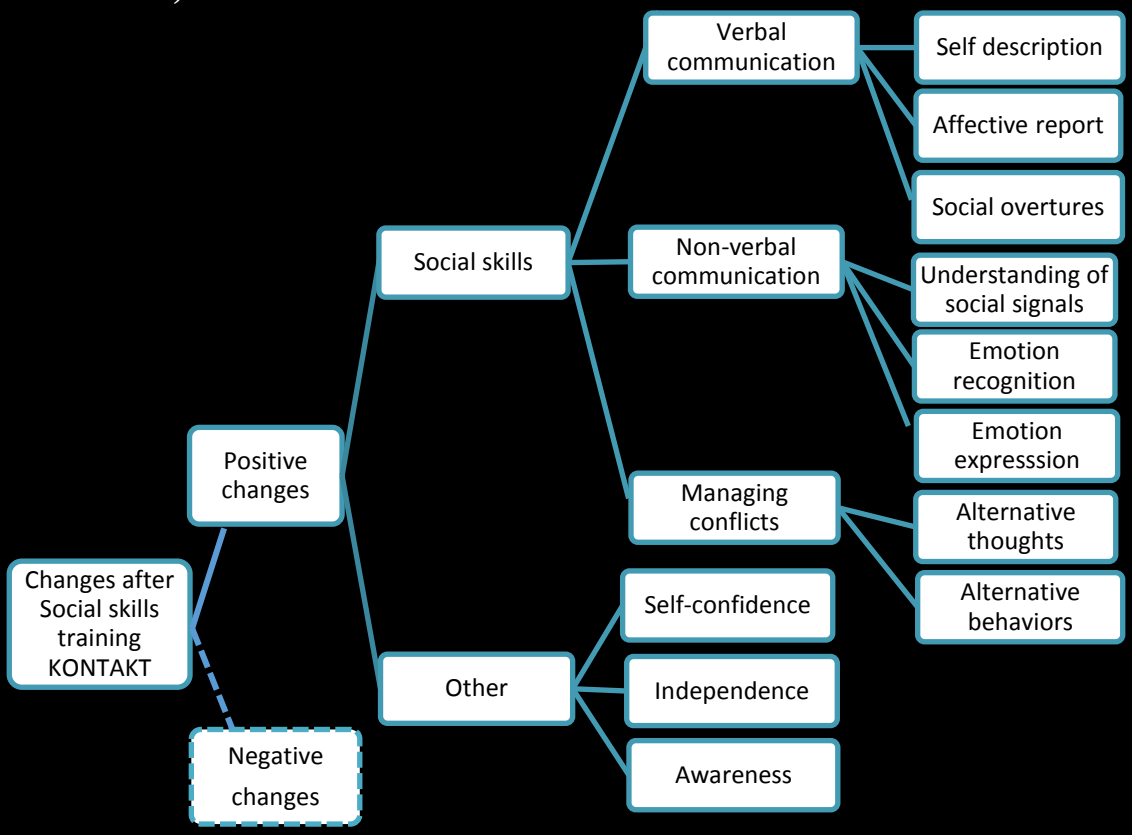


4.4 STUDY IV. QUALITATIVE EVALUATION OF SSGT- KONTAKT

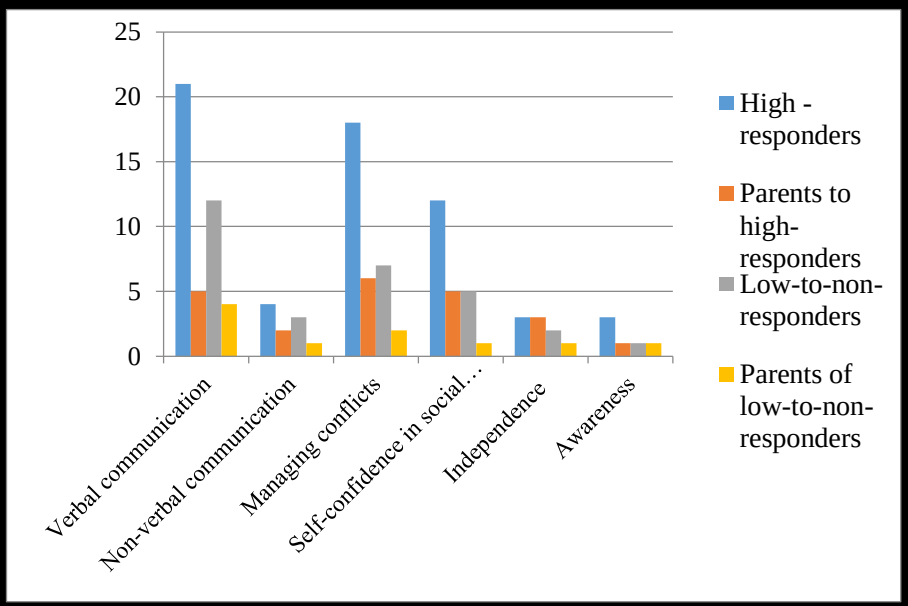
Results according to participants following KONTAKT and their parents showed that KONTAKT contributes to improved social skills, increased awareness of one's own impairments, higher self-confidence, increased independence, and a new way of thinking about consequences (Figure 5).

Figure 5. Results of the thematic analysis

a) Themes and subthemes



b) Frequency for each subthemes



There were no differences in reported effects between high-responders and low-responders, and even low-responders expressed benefits from the treatment. Good group cohesion and a positive attitude toward homework assignments were associated with larger treatment gains. According to participants and parents, KONTAKT needed to be of longer duration.

5 CONCLUSIONS ABOUT EACH RESEARCH QUESTION

The overall objective of this research was to evaluate the efficacy and effectiveness of SSGT-KONTAKT for children and adolescents with HFASD and psychiatric comorbidity. We divided the thesis into two parts:

Prior to the trial: The method was confirmed in Study I, whit the objective of exploring and inventorying prior RCT studies on SSGT for children and adolescents with ASD, focusing on the external validity, and Study II, with the objective of evaluating the clinical utility and interrater reliability of two tools (the Swedish version of DD-CGAS and OSU Autism CGI-S used in PRCT). *Studies related to the trial*: These aimed to evaluate the efficacy and effectiveness of SSGT-KONTAKT for children and adolescents with HFASD with psychiatric comorbidity when implemented in naturalistic outpatient care (Study III) and to evaluate participant experiences about the treatment and their parents' experiences after participating in SSGT-KONTAKT (Study IV). Below, I turn to the conclusions of each study.

5.1 STUDY I

As indicated in the introduction, prior RCT studies there have involved several methodological limitations and knowledge gaps in regard to the external validity of the study of SSGT. The review provided in Study I revealed that the generalizability of the accumulated evidence is unclear and that the determinants of external validity are often inadequately reported. More effectiveness oriented RCTs of equally high internal and external validity are needed. More attention to the determinants of external validity is warranted when this new generation of RCTs is planned and reported. Based on the results of the review, a checklist was developed to facilitate evaluation of external validity of trials and better report this information in future studies. This checklist was used to examine both the efficacy and effectiveness of SSGT-KONTAKT (12 sessions) in Study III (checklist, Appendix 2).

5.2 STUDY II

Study II yielded several outcomes. First, it demonstrated that both the DD-CGAS and OSU Autism CGI-S are feasible tools for quick and general assessment of symptom severity and psychosocial functioning in ASD. Second, in a heterogeneous naturalistic clinical setting the DD-CGAS and OSU Autism CGI showed sufficient inter-rater reliability without explicit a priori training. Third, agreement was substantial between

raters with clinical experience working with individuals with ASD compared with those with less experience. Fourth, DD-CGAS and OSU Autism CGI-S hold promise for a broad range of clinical and research purposes in ASD, particularly outcome evaluation. Finally, DD-CGAS and OSU Autism CGI are equivalent, showing a high inverse correlation between these instruments.

5.3 STUDY III

The findings of Study III indicate that SSGT KONTAKT (i) is feasible in naturalistic clinical settings, (ii) shows significant effects on social cognition and several adaptive skills and abilities as well as better every-day functioning and decreased symptom severity in both groups, and (iii) has greater effects in adolescents. Furthermore, (iv) results for post training vs. follow-up indicate that some effects are lost without ongoing intervention, (v) parents report more improvements than teachers, (vi) parent stress particularly in the children group decreased after the treatment, and (vii) the treatment has no significant effect on participants' perceived stress.

5.4 STUDY IV

Even participants not showing noteworthy improvements on a primary quantitative outcome measure ("low-to-non-responders") reported treatment satisfaction and positive intervention effects, although to a lesser extent than "high-responders." This finding suggests that non-responders obtained benefits from the treatment that are not captured by quantitative measures. Feedback from participants and relatives provides valuable insights for further improvements of manualized SSGT.

6 DISCUSSION

Despite widespread use in clinical practice, the evidence on the efficacy and effectiveness of SSGT is still not sufficient. Development of SSGT programs and evaluation of these programs has improved since the first qualitative study on SSGT was conducted in the 1980s (Mesibov, 1984). Efficacy studies of SSGT using RCTs have shown small to moderate effects, but several methodological problems remain to be improved (Kaat & Lecavalier, 2014; Reichow, Steiner, et al., 2012; Williams et al., 2007). The results of the studies described in this thesis suggest that both KONTAKT+TAU and TAU only have a significant effect over time. There were also found a significant effect of KONTAKT in parent-rated social responsiveness skills, particularly social cognition, and some social adaptation skills, predominantly in adolescents compared with the control group. However, no significant effect on teacher rating was found. The study also showed that participants who received KONTAKT showed significant effects in everyday functions and decreased ASD symptoms according to clinician ratings. The strength of the study is that we used a large sample size (N=296), and participants with psychiatric comorbidity, recruited from current health care, with clear inclusion and exclusion criteria, and

information on randomization, blind assessments, and outcome measures related to social skills, adaptive skills, and every day function to measure the generalizability of acquired skills. The study showed general satisfaction among participants in both the child and adolescent groups, where both responders and non-responders indicated positive experiences of participating in the treatment.

Study I also illustrated methodological limitations in regard to external validity or effectiveness of SSGT programs in real world health care and pointed to specific areas to improve, such as limited information about the inclusion of participants with comorbidity, location, and settings, and information about the recruitment process. However, inadequate information regarding the determinants of external validity could considerably reduce the applicability of the trial results and ultimately lead to a waste of resources allocated to research (Glasziou et al., 2014). Study I suffered from several limitations, as follows: 1) Limited sample size: as a consequence of the eligibility criteria we found only 15 studies. The objective of the study was to explore RCTs with sufficient internal validity, which is an indispensable prerequisite for external validity (not vice versa). 2) Only information provided in the primary research report was reviewed. We did not contact authors for missing information, nor did we review all possibly available literature and information outside scientific journals.

In spite of these limitations, the information acquired in this study allowed the authors to develop a checklist with the aim of improving the external validity of future RCT studies particularly in our multicenter PRCT in study III.

Study II was focused on validation of two tools, DD-CGAS and OSU Aut CGI-S, which were employed in the multicenter PRCT, allowing use of evaluated outcome measures as recommended in several reviews (Kaat & Lecavalier, 2014; McMahon, Vismara, & Solomon, 2013; Reichow, Steiner, et al., 2012; Williams et al., 2007) of the clinical applicability of these tools in naturalistic settings. The results showed that experienced clinicians had better agreement compared to inexperienced clinicians and suggested that the results of the two tools inversely correlate. This study had the following limitations: 1) we focused on interrater reliability, and no other aspect of reliability or validity, however, the study was embedded in Study III, and we focused on the degree of agreement to consider the applicability of the tools in the trial; 2) clinical vignettes were used that were based on real children and adolescents with ASD and comorbidity, described typical clinical pictures before and after treatment, and was not based on current patients; 3) the observable change in the vignettes was moderate, and despite this possibly being characteristic of ASD over a shorter period of time, the sensitivity of the DD-CGAS and OSU Aut. CGI-S to change could therefore be demonstrated only to a certain degree.

For studies III and IV, the main objective was to evaluate both the efficacy and effectiveness of SSGT-KONTAKT. For this purpose, we used a mixed convergent method (quantitative and qualitative studies).

Quantitative study

In study III, we attempted to overcome the methodological flaws found in prior RCT studies. To achieve better results regarding the efficacy and effectiveness of SSGT, some methodological considerations were incorporated. We used a large sample of 269 participants with ASD and psychiatric comorbidity. The participants were recruited and trained in 14 regular clinical settings. We defined the primary and secondary outcome measures to test the effect on not only social skills, but also adaptive behavior, everyday functioning, and symptom severity. For these purposes, we applied a computerized block randomization and prior evaluated manualized SSGT program.

In general, the results showed a moderate effect of SSGT-KONTAKT according to the parent ratings in SRS. Interestingly, both the KONTAKT and TAU groups showed better results considering time effect, while the blinded teacher rating showed no significant effect. Looking at the subscales, the study results suggest that KONTAKT has a significant effect on social cognition at both post treatment and follow-up, showing that the effect remains 3 months after treatment completion. In the age-group analysis (children and adolescents), KONTAKT seems to have had a better effect in the adolescent group in several areas of adaptive skills. Furthermore, the child group showed improvements in every day functioning, and decreasing symptom severity compared to the adolescent group and their control group, respectively, according to clinician ratings. The perceived stress of the parents decreased in both groups, but no effect was found in perceived stress in either the child or adolescent group.

Despite some evidence of effect of SSGT-KONTAKT, the study had several limitations, as follows: 1) the parent rating showed better results than those of the blinded teacher ratings, which could have significance for the research findings. Parents' better knowledge of the treatment could have resulted in a bias. On the other hand, the teachers had not been trained, and they often reported that they could not answer the questions in the questionnaires because they did not have sufficient knowledge about the participants' social abilities and the time to focus on one student; 2) the study did not use an objective outcome measure. We used questionnaires that were rated by parents, teachers, clinicians, and the participants themselves. Such questionnaires suffer from the subjectivity of raters, which influences the evaluation of the treatment effect; 3) despite finding some effect of SSGT-KONTAKT; the mechanisms of the treatment effect have not yet been analyzed. Several reviews have also recommended the need for studies in regard to moderator and mediators of the treatment effect, e.g., group cohesion and time duration. One of the ongoing studies involving KONTAKT is to examine whether the time duration of the treatment delivery influences the treatment effect; 4) the data analysis was based on the intention-to-treat principle, with mixed effect modeling. This method allows including all participants from both experimental and control groups to handle the drop-out issue. It takes in to account the fixed and random data, and the study is based on likelihood analysis. Although the drop-out problem in this type of study is common, a future

improvement could be to have better and easier outcome measures, that take in to account the limited time the raters have; 5) the study did not analyze whether treatment effects depend on variables, such as sex, age, intellectual skills, comorbidity, language level, medical history, ongoing concurrent treatments, and genetic variation to determine whether some treatments work in certain individuals. These analyses are planned for upcoming studies based on the database of Study III. The goal is to explore the significance of these variables for offering better care using personalization measures, such as genetic markers, which could give patients with ASD, and clinicians the possibility of choosing those individuals who are likely to respond. Personalized medicine holds great promise for improving clinical effectiveness, reducing costs, and increasing therapy safety.

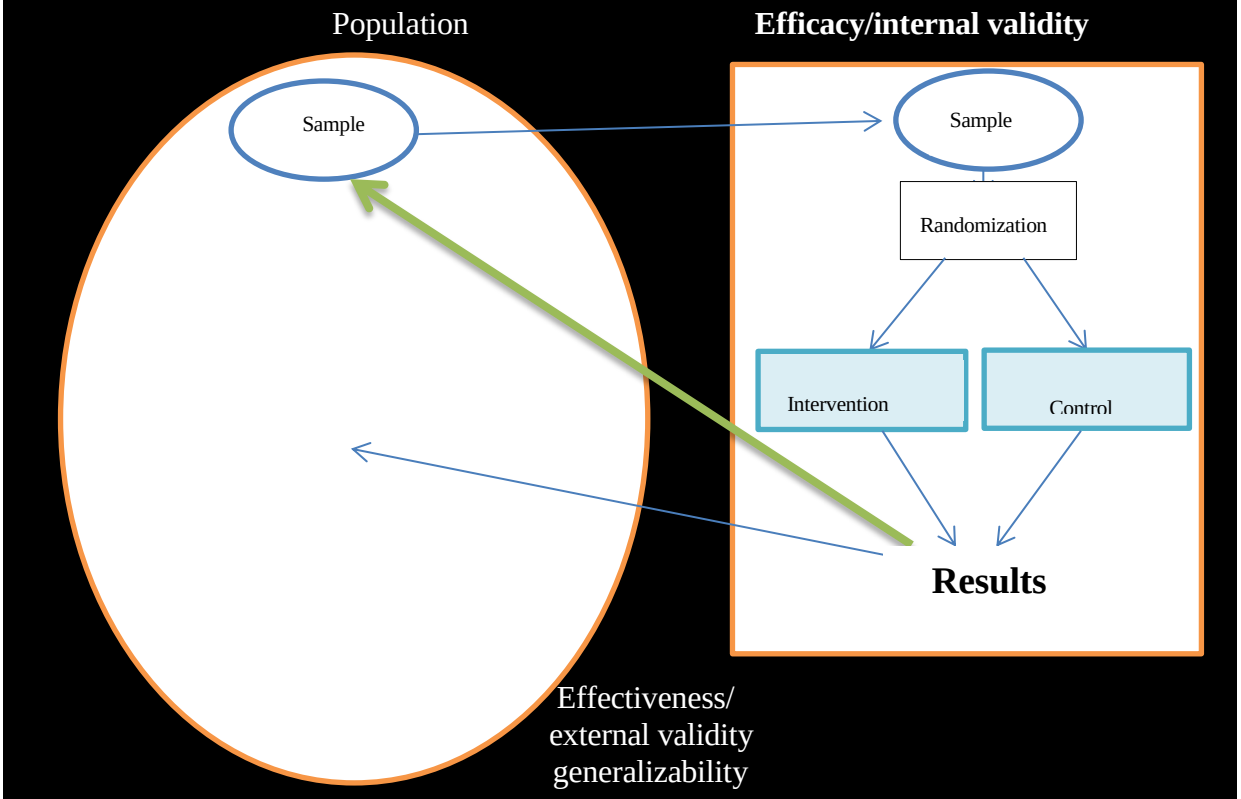
The qualitative study

Study IV was aimed at investigating perceived treatment-related changes following participation in KONTAKT by interviewing children and adolescents with HFASD (and their parents) who showed high effect (responders) and low effect (non-responders) with improvements in social skills and other areas of functioning. Moreover, the reported experiences provide information about the possible composition of social skills and other changes, such as self-description skills, understanding social signals, emotion processing, alternative thoughts and behaviors, increased self-confidence, independence, and awareness of one's own difficulties. Particularly, awareness of one's own difficulties has been considered an important factor for positive SSGT outcomes (Chang et al., 2014; Lerner, White, & McPartland, 2012).

Several limitations of the current study need to be addressed to judge its validity and the generalizability of findings, as follows: 1) the sample size might be considered small, however, for qualitative research, as mentioned earlier, a data collection of 22 interviews is usually sufficient to approximate saturation. Nevertheless, there are no defined criteria to determine when saturation is reached, and saturation is ultimately unable to prove in itself that it leads to exhaustive results; 2) the interviews were conducted approximately one year after the end of treatment, so recall bias must be taken into account (Bölte et al., 2006), but, we can consider that the perceived effect of KONTAKT for both participants and parents seems to be maintained a year after the treatment; 3) the difficulties in communication and abilities in verbal expressiveness in individuals with ASD (Losh & Gordon, 2014), might limit access to comprehensive verbal data about the perception of SSGT; 4) some of the low responders dropped-out during the recruitment of study participants. One of those who chose not to participate in the study expressed negativity towards the group, according to the parent. Thus, owing to drop-out, the present findings might be overly positive, and more negative voices might have been missed; and 5) parent-report SRS scores were used to classify high and low responders within the framework of an ongoing PRCT of SSGT-KONTAKT. To what extent parent SRS scores alone can access true "responding" to SSGT is uncertain.

In conclusion, clinical trials conducted in community practices allow researchers to face several methodological challenges related to maintaining a balance between internal validity and external validity, and generalizability (Lurie & Morgan, 2013; Thorpe et al., 2009). Nevertheless, using PRCT, which takes in to account both internal and external validity and using the CONSORT guidelines (Appendix 1) and "Checklist for reporting external validity information in RCT studies" (Appendix 2), we believe that a high research quality of PRCT is possible (Figure 6). In addition, quantitative studies, such as RCTs, which are considered the gold standard, are likely to be insufficient, because outcome measures such as SRS do not capture different areas of treatment feasibility and effectiveness (Dattilio et al., 2010; O'Cathain et al., 2013). RCTs alone, cannot provide a basis for the detailed decisions that practitioners must make in the face of the complexities of individual cases (Dattilio et al., 2010), and qualitative studies can give complementary and important information to quantitative studies(Brown, 2001; Bölte, 2014b; O'Cathain et al., 2013). In the studies presented in this thesis, we used the convergent mixed method which is necessary to evaluate treatment effect and involves participants' views about treatment strengths and limitations according their perceived experiences (Figure 7).

Figure 6. a) Randomized controlled trial (RCT)



b) Pragmatic randomized controlled trial (PRCT)

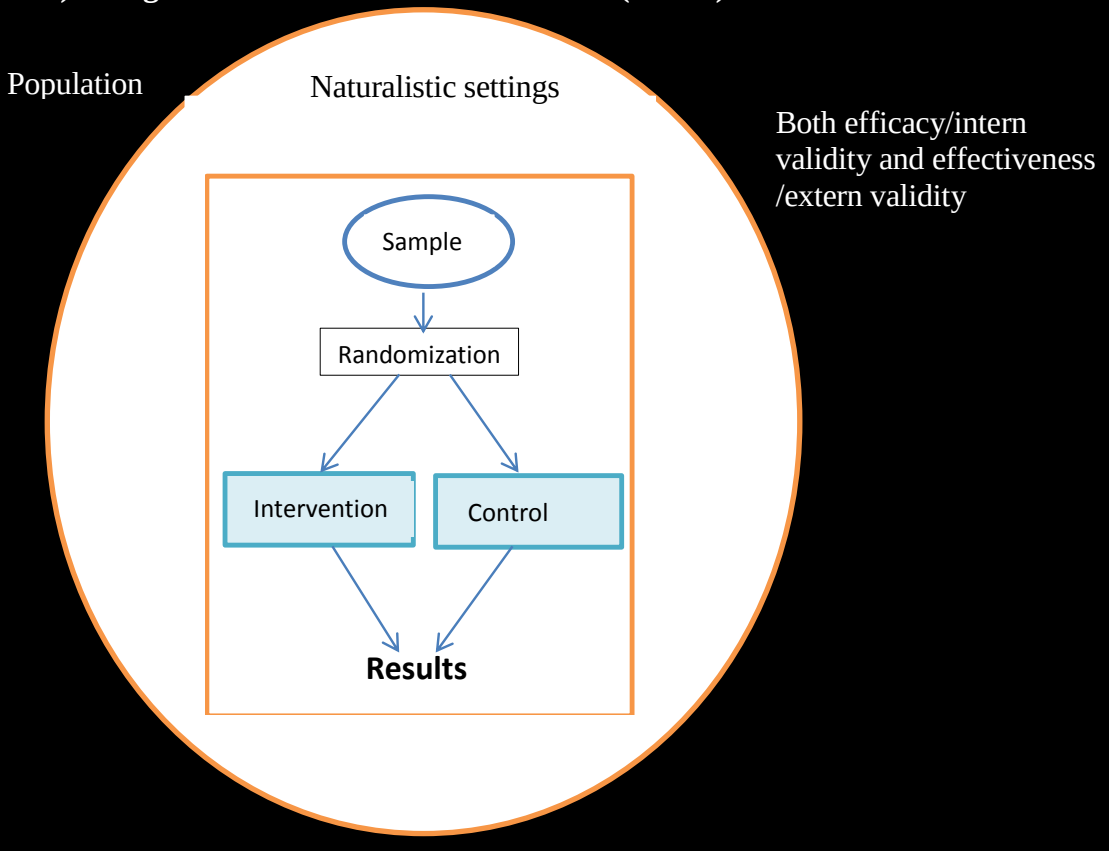
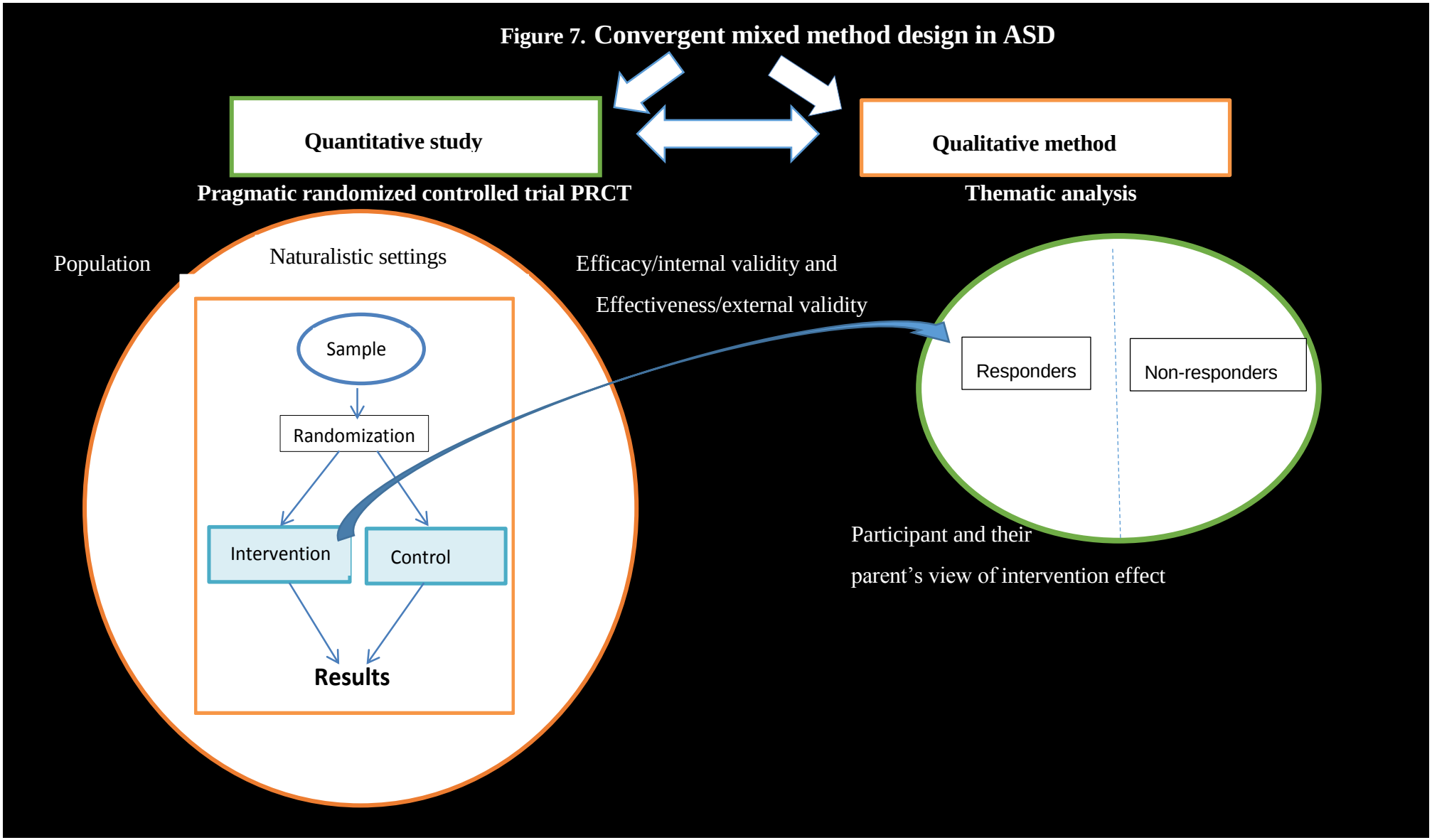


Figure 7. Convergent mixed method design in ASD



7 IMPLICATIONS FOR FUTURE RESEARCH ON INTERVENTIONS AND CLINICAL CARE OF ASD

Implications for future research

Effectiveness and efficacy are two concepts that researchers, treatment providers, and clinicians have used to describe the effects of an intervention in clinical research. Researchers, clinicians, policy makers and patients have focused on the effect of an intervention, looking at it from different angles and prioritizing questions related to its efficacy and effectiveness. Researchers are interested in whether the intervention can achieve the intended effect (efficacy) whereas clinicians and policy makers want to know whether it achieves the intended effect in real world health care (effectiveness). In addition, patients are interested in whether or not the intervention is efficient for them as individuals (experiences and views of participants following the intervention).

Several attempts have been made during the last 20 years to evaluate a treatment program or intervention, but the efficacy and effectiveness of a treatment are still not being sufficiently evaluated. As described in the Introduction, some improvements have been made using RCT studies to test the efficacy of SSGTs, and effectiveness is almost neglected. On the other hand, several SSGTs are used in the clinical settings that are considered feasible without rigorous evaluation. In addition, no studies have examined what the participant considers to be the utility of these treatments.

To assess the efficacy and effectiveness of KONTAKT, we used a convergent mixed method approach (quantitative and qualitative) with a multicenter PRCT design and responder and non-responder analyses. We had a large sample size of 296 participants recruited and treated in 14 community-based child and adolescent settings located in Stockholm and Örebro. All participants were recruited from regular health care, where they were, being treated by current clinicians. We also interviewed responders and non-responders among those who participated in the treatment. The thesis findings suggest that it is possible to investigate the efficacy and effectiveness of SSGT using a mixed method approach and taking into account researchers, clinicians, policy makers, and patients with ASD to obtain results with maximum likelihood and make it easier to generalize to current health care.

The results might hold promise for a range of purposes in outcome evaluation of future PRCT studies, evaluating intervention for children and adolescents with ASD, and working closely with clinicians and patients. It is necessary to improve in the following areas:
1) Implement blinded raters who have sufficient information or access to evaluate whether the treatment has an effect or not. One suggestion could be to blind clinicians.
2) Standardized objective measurements are needed to improve measurement of the treatment impact using other methods (e.g., computerized questionnaires or computer-based outcome measures easy to access for this population).
3) Examine the significance for treatment effect of moderating factors such as genetic

predisposition, age, IQ, gender, verbal skills, and comorbidity.
4) Investigate the significance for treatment effect of mediators such as time duration of treatment delivery and treatment adherence.
5) Evaluate the sensitivity and specificity and the interrater reliability of DD-CGAS and OSU Aut CGI-S using current patients.
6) Implement and replicate the study in the CAMHS, CAHS and other mental health clinics in Stockholm and other regions to confirm the effectiveness of KONTAKT as well as in the schools.

Implication in clinical praxis

Since 2010, CAMHS in Stockholm county has developed guidelines to offer better evidence-based and effective practices in diagnostics and intervention for children and adolescents with ASD (Choque Olsson et al., 2012). The guidelines have been updated, but interventions for this population are still scarce. The KONTAKT research project has been started based on the need for alternative evidence-based interventions. As mentioned in studies III and IV, KONTAKT has been successfully implemented in 11 clinics at CAMHS in Stockholm, one private Child and Adolescent psychiatric clinic, and one clinic at CAHS in Örebro. The study showed a significant effect on some social skills among patients with ASD and comorbidity. Study II showed the importance of the degree of experience in the evaluation of treatment effect, with more agreement among experienced clinicians than among those with less experience.

Within the mental health care system, systematic and structured monitoring of processes and patient outcomes is needed to ensure quality of care and patient safety. Studies II, III, and IV have allowed clinicians to be part of a large study and work systematically according to the treatment curriculum and the importance of evaluating the effect of the treatment. However, current electronic medical records and systems are mostly used for administrative purposes and evaluate only the frequency of the treatment delivered, not the treatment effect. A better quality registry for diagnostic and treatment outcome is needed, which can offer a basis for a discussion about best practices, providing future transparency in treatment outcomes and quality indicators between healthcare providers and allowing easy communication with patients and caregivers regarding the alternative interventions in ASD and other neurodevelopmental disorder. For this purpose, in line with a recent RCT study (Freitag et al., 2015) adapted and standardized clinically feasible instruments to measure observation of changes are needed.

Participants' own views

In addition, both patient and parent views of the treatment effect of KONTAKT were satisfactory. This study is the first to focus on the participant view of the effect and content of a treatment combined with a quantitative analysis, which is lacking in research and treatment in ASD (Grant, Rodger, & Hoffmann, 2015; Pellicano et al., 2014). Study III showed the need for better adaptation of KONTAKT for the child group, and study IV

showed the potential for treatment improvement regarding content. Patient and parent involvement in treatment of children and adolescents with ASD is necessary, and a systematic analysis of their perception in combination with a rigorous quantitative evaluation using PRCT could give better information regarding treatment efficacy and effectiveness.

8 OVERALL CONCLUSIONS OF THE THESIS

The overall conclusions of this thesis are summarized as follows: (1) More studies on both internal and external validity and the generalizability of SSGT in ASD are needed. (2) SSGT-KONTAKT (12 sessions) can be successfully implemented in "real-world" clinical health care. (3) KONTAKT+TAU is more efficient in some areas of social responsiveness compared to only TAU, according to the parental perspective. (4) KONTAKT has a better effect in adolescents in regard to social communication, social motivation, and social cognition and a better effect in children for everyday functioning and symptom severity. (5) No significant effect was identified from teachers who were not aware of which group the student participated in. (6) The intervention has a positive impact on parents' perceived stress in the child group. (7) KONTAKT has no impact on the perceived stress among the children and adolescents. (8) KONTAKT needs more adaptation for child groups. (9) The intervention is effective from the perspectives of high and low-responder participants. (10) DD-CGAS and OSU Aut CGI are useful for measuring change effects of clinically delivered treatment in ASD.

In conclusion, more studies with a convergent mixed method approach to assess efficacy, effectiveness, and participant experiences following SSGT are necessary to support more robust conclusions. KONTAKT could be an effective and efficient complement to treatment as usual in regular clinics for children and adolescents with ASD, and the intervention may significantly increase access to evidence-based care.

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Appendix 1.

CONSORT 2010 checklist of information to include when reporting a randomized trial*

Section/ Topic	Item No	Checklist Item	Reported on page No*
Title and abstract			
	1a	Identification as a randomized trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4, eA[a] 1
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5, eA 1
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6, eA1
	6b	Any changes to trial outcomes after the trial commenced, with reasons	-
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	7
Randomization			
Sequence generation	8a	Method used to generate the random allocation sequence	4 eA1
	8b	Type of randomization; details of any restriction (such as blocking and block size)	eA1
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps	4 eA1

		taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	eA1
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	6
	11b	If relevant, description of the similarity of interventions	-
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	7
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	8
	13b	For each group, losses and exclusions after randomization, together with reasons	8
Recruitment	14a	Dates defining the periods of recruitment and follow-up	eA1
	14b	Why the trial ended or was stopped	-
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	8, T[b]1,2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	8, T[b]3,F[c]1,
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	8, eA2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	-
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	9-10, T[b]3,eA2
Harms	19	All-important harms or unintended effects in each group (for specific guidance see CONSORT for harms), *adverse events*	6
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	11
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	11

Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	11
Other information			
Registration	23	Registration number and name of trial registry	2,4
Protocol	24	Where the full trial protocol can be accessed, if available	4
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	0

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomized trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.www.consort-statement.org.

* Checklist used in the Study III, see the manuscript for more information.

[a] eA= Appendix in the supplement; [b]T=Table, [c]F=Figure

Appendix 2.

Checklist for reporting external validity information in RCT studies

Items	Comment	Example (information included in the trial report by Frankel et al., 2010)[a]	Reported on page No*
Source population			
1.Primary diagnosis	Criteria and methods used to confirm the diagnosis	Autism spectrum disorder according to ADOS, ADI-R and ASSQ	6
2.Additional inclusion criteria	Any additional inclusion criteria	Verbal IQ ≥60; able to switch topics in a conversation; adequate knowledge of rules in playing and common school yard games; attending 2nd through 5th grade regular classroom	4
3.Exclusion criteria	Any exclusion criteria	Prescribed psychotropic medication; clinical seizure disorder; thought disorder	4,5
4.Recruitment plan and type and procedure of recruitment (e.g. advertise-ment, clinic referral)	Detailed description of the recruitment plan enabling identification of the source population (e.g., the clinic's catchment area and the type of patients referred to the clinic)	Parents calling to the UCLA Outpatient Clinic about the social skills program or parents evaluated by the Assessment Core of the UCLA Center for Autism Research and Treatment	4, eA1
Included population			
1.Sample selection	The number of individuals approached for participation, screened, randomized, and completing the trial	Approached: not reported screened: not reported; randomized: 76; completed: 68	4,8, F1, eA1
2.Age	Mean (SD) and range	6 -11 years; treatment/control mean =8.4/ 8.6	8, T[b]1
3.Sex	Number of males and females included	58/10	8 , T[b]1
4.Comorbidity	The psychiatric and somatic comorbidity of the participants	Not reported	4
5.Additional sample characteristics	Baseline characteristics of the sample, such as diagnosis, social skills, socioeconomic status, IQ, ethnicity, and ongoing treatments	ASD diagnosis: Social skills: SSRS–assertion, treatment/control, mean (SD) =9.5 (2.8)/9.4 (3.4) IQ: Verbal IQ, treatment/ control, mean (SD) =106.9 (19.1)/100.5 (15.7) Parent education: - Ethnicity: Caucasian, treatment/control =77.1/54.5% Psychotropic medication: Excluded	7,8, T[b]1,2
6.Treatment preferences and expectations	Information about the participants treatment preferences and expectations (e.g., choice of treatment and motivation)	Not reported	-
Context			
1.Location	The geographical area in which the study occurred (e.g., city, country, region)	Los Angeles, California, USA	4
2.Concurrent secular events/timing	The time period of data collection (e.g., month and year) and external events occurring at the time of the intervention that could influence outcome	Recruited from Sept. 2003 to March 2008	eA2

3.Setting type/service environment	The type of settings of data collection in the study (e.g., classroom, participants' homes, clinic, university clinic); service provider, characteristics of the service environment (e.g., economic, legal, political, demographic, technological, and policy-related environment; availability of alternatives outside the trial context; compensation structures; unique features of the trial environment)	Regular outpatient clinical service	4, eA1
4.Number of settings	Different settings of data collection in the study (e.g., number of classrooms, participants' homes, clinics)	Not reported	eA1
5.Ethics	Information, consent	Approved by the university and the NIMH IRB. Parent consent and child assent.	4
6.Incentives	Any incentives or compensation for participating in the trial	Not reported	eA1
Treatment provider			
1.Number of providers	Number of professionals and teams delivering the intervention	Teams: 1 (+ 1 for parents groups) Therapists/team: 1	eA1
2.Staffing	Actual staffing of the intervention (i.e., number and qualification of the staff involved)	PhD level psychologist with ≥ 10 years of experience (licensed clinical social worker with ≥ 5 years of experience in the parent group)	eA1
3.Provider training	How intervention providers were trained	10 years of experience in social skills training	eA1
4.Supervision	Any contacts between intervention providers and supervisors/researchers	Not reported	eA1
5.Treatment fidelity	Steps to measure adherence of care providers with the protocol (e.g., incentives for staff compliance, participant feedback, mailings or phone reminders)	Fidelity checklists covering the primary content of the protocol created for each treatment session	eA2
6.Provider preferences	Information about treatment preferences of providers (if more than one treatment option is available)	Not reported	-
Treatment intervention			
1.Intervention manual	Information for accessing intervention materials (e.g., protocol or manual) to allow for replication	Parent-assisted Children's Friendship Training (CFT), (Frankel and Myatt 2003). Parents integrated within separate concurrent sessions	5, eA1
2.Composition of groups	Number of groups and group size	Usually 10 in each group, whereof a maximum of 4 with autism spectrum disorder	5, eA1
3.Duration	The intended length of the intervention (e.g., 20 week programe)	12 weeks	5, eA1
4.Frequency	The frequency of intervention (e.g., 1 per week)	Weekly	5, eA1
5.Intensity	The intended intensity of the intervention (i.e., length of each session)	60 min	5, eA1

6.Costs	Any costs associated with the treatment (e.g., cost related to material, staff, supervision, training)	Not reported	No reported
7.Deviation/tailoring	Intervention adaptation by researchers and staff (e.g., types and extent of deviations from protocol that have not been highlighted above, including supplementing the treatment)	Not reported	-
Outcome			
1.Type of data	Qualitative and/or quantitative, scales, tests, observations	Quantitative data Rating scales	5
2.Informants and measures	The primary and secondary outcome measures (including informant for each measure) and the informant for each measure (e.g., child, parent, staff, teacher)	Child: The Loneliness Scale, Piers-Harris Self-Concept Scale Parent and Teacher: QPQ, PEI Staff: SSRS (primary outcome)	5
3.Generalizability and quality of outcome measures	Method of data collection, on site results for reliability and validity, enactment of learned skills in relevant real-life settings	Multiple sources: yes; observations by blinded raters: no; any blinded assessment: no; on site reliability or validity data: yes, for QPQ Enactment:	8-10
4.Timing of measurement	The timing of measurement and follow-up period for all groups and measures in the trial	Just prior to receiving the intervention (T1), the last night of the intervention (T2), and 12 weeks after the conclusion of the intervention (T3). Follow-up after 1-5 years presented in a more recent publication	eA1
5.Authors' view on generalizabili-ty	Any discussion referring to generalizability of the results	Findings limited to a select subsample of high functioning children with autism spectrum disorders	10,11

* Checklist used in the Study III, see the manuscript for more information.

[a] eA= Appendix in the supplement; [b]T= Table, [c]F= Figure

Appendix 3.

Children's Global Assessment Scale for Developmental Disabilities (DD-C-GAS)

Skatta personens funktionsförmåga inom de viktigaste områdena såsom exempelvis: a) ADL, egenvård, mat, påklädning, sömn, b) kommunikation, c) sociala beteenden samt d) studieresultat och fungerande i hemmet, skolan och i social gemenskap. Skatta personens funktionsnivå genom att välja de nivåer som presenteras nedan i förhållande till barnets/ungdomens normala utveckling och jämfört med jämnåriga. Använd även de intermediära nivåerna (t.ex. 35, 58, 62).

Skatta aktuell funktionsförmåga utan hänsyn till behandling eller prognos. De tillhandahållna exemplen på beteenden är enbart illustrativa och erfordras inte för en speciell skattning.

Namn:_____ Datum:_____

Specificerad tidsperiod: 1 månad

100-91 Synnerligen god funktionsförmåga inom alla områden (hemma, inom familjen, i skolan och med kamrater). Är engagerad i flera aktiviteter och har god förmåga att upprätthålla intressen (t.ex. har fritidsintressen och deltar i eller tillhör organiserade grupper såsom scouterna etc.). Klarar sig bra i hemmet, skolan/arbete. Inga tecken på någon form av funktionsnedsättning.

90-81 Fungerar tillfredsställande inom alla områden (hemma, inom familjen, i skolan och med kamrater). Det kan förekomma tillfälliga svårigheter och vardagsbekymmer som ibland blir ohanterliga eller resulterar i känslomässigt lidande på grund av funktionsnedsättningar (t.ex. i form av oförutsedda förändringar i dagliga rutiner eller i den fysiska miljön). Har tillfredställande adaptiva färdigheter i hemmet, skolan/arbete och har en fungerande vardag.

80-71 Endast lindriga funktionssvårigheter (hemma, inom familjen, i skolan och med kamrater)**.** Mestadels ett åldersadekvat beteende. Mindre förändringar i vardagliga rutiner eller i miljön kan orsaka tillfälligt nedsatt och bristande funktion. Sociala kontakter kan vara ensidiga och utgå från intressen snarare än genuin nyfikenhet eller intresse för relationer/interaktion. Språket och kommunikationen är åldersadekvat men samtal kan upplevas vara ensidiga. Ofta krävs påminnelser och uppmaningar för att dessa barn/ungdomar skall få en fungerande struktur i vardagen såsom i hemmet, skolan/arbete. Dessa barn/ungdomar kan vara lite mer omogna än jämnåriga, men anses inte vara avvikande.

70-61 Medelsvåra funktionssvårigheter inom ett enstaka område, men fungerar allmänt sett ganska väl. Nedsatt social förmåga i vissa situationer. Lär sig lämpliga sociala färdigheter, men kan vara rigid och ha bristande förmåga att generalisera. Nedsatt adaptiv förmåga inom några områden. Märkbart avvikande beteende i vissa situationer (t.ex. i sociala grupper, på ostrukturerade tillställningar) som påverkar social acceptans. Har få och/eller begränsad delaktighet i aktiviteter som är åldersadekvata på ett eller två områden eller i en specifik situation. Begränsad deltagande i hemmet, skolan/arbete.

60-51 Medelsvåra funktionssvårigheter inom de flesta områden. Behöver avsevärda struktur och tillsyn för att klara av vardagliga rutiner. Dagliga livet/adaptiva färdigheter är under åldersnivån. Kommunicerar sina behov, svarar mot grundläggande önskemål (verbalt eller ickeverbalt). Det verbala förmågan (språk om det finns) är stel och försenad. Sociala begränsningar och/eller ovanliga beteenden som är tydliga i de flesta miljöer och som bidrar till ett fungerande under vad som förväntas för åldern i hemmet, skolan/arbete.

50-41 Medelsvåra funktionssvårigheter inom de flesta områden och grav nedsatt funktion i minst (ett område) en domän (t.ex. dagliga livet eller kommunikation). Social kontakt och/eller svar på omgivningens försök att kommunicera är markant avvikande eller olämplig. Vardaglig kompetens är väsentlig försenad (t.ex. klä på sig, sköta hygien, äta). Stereotypa och eller andra ovanliga beteenden är märkbara för en ytlig betraktare i hemmet, skolan/arbete.

40-31 Grava funktionssvårigheter inom flera områden. Outvecklad/ rudimentär eller instrumentell (ej social) kommunikationsförmåga. Repetitiva beteenden som begränsar den adaptiva förmågan. Påtagligt socialt tillbakadragande och isolerat beteende i de flesta situationer. Den adaptiva beteendeförmågan är betydlig mer begränsad än jämnårigas. Behov av omfattande stöd från omgivningen i vissa områden. Omogen anpassningsförmåga och egenvård och begränsade färdigheter inom minst två områden: hemmet, skolan/arbete

30-21 Grava funktionssvårigheter inom alla områden (t.ex. hem och skola). (Oförmågan att fungera inom nästan alla områden) Påtaglig tillbakadragande och isolerat beteende. Kräver omfattande stöd av omgivningen och miljö-boende (t.ex. intensiv beteendeträning samt anpassad boende: låsa skåp, ta bort farliga objekt från rummet). Beroende av andra i alla aspekter i vardagen såväl i hemmet som i skolan/arbetet (t ex. påklädning, bad, toalettbesök). Långt under förväntan åldersmässigt. Kan uppvisa störningar av grundläggande färdigheter (t.ex. sömn, matvanor rutiner och regleringsförmåga).

20-11 Extrema funktionssvårigheter i minst ett område (kräver ansenlig tillsyn och övervakning). Behov av kontinuerlig övervakning, eller omfattande miljö-boende för säkerheten, eller för grundläggande vård och hygien (t.ex. matvanor, toalettbesök). Behöver placeras i ett hem/gruppbostad med tillsyn och stöd. Förmedlar inte grundläggande behov. Interagerar inte med andra. Påtaglig störning av grundläggande behov (t.ex. sömn, mat, etc).

10-1 Extrema och genomgående funktionsnedsättningar (kräver ständig tillsyn och övervakning). Är en fara för sig själv eller/och andra. Behov av intensiv och ständig övervakning (t.ex. 24-tim vård utanför hemmet) för andras och egen säkerhet. eller totalt beroende av hjälp för grundläggande behov (t.ex. hygien, nutrition, toalettbesök etc). Påtaglig störning av reglerings färdigheter. Behöver specialiserad vård (t.ex. uppförande förvaltning eller sjukvård) utöver vad som kan ges i hemmet.

Nora Choque Olsson & Sven Bölte (2011) efter Wagner et al. (2007), BIOL PSYCHIATRY; 61:504–511; *DD-CGAS som är baserad på/anpassad från Children's Global Assessment Scale (Shaffer et al, 1983) och Global Assessment Scale (GAS, Endicott et al, 1976).*

Appendix 4.

OSU Aut CGI-S
Skala för den globala kliniska bilden vid autismspektrum
Bedömning av symtomens svårighetsgrad (S) och
bedömning av förändring/ förbättring (I) vid uppföljning

Alane Kadouri, Emmanuelle Corruble et al., (2007)
Svensk version: Nora Choque- Olsson & Sven Bölte

Denna skala används för en övergripande klinisk bedömning av den totala svårighetsgraden av symptomen i samband med autismspektrumtillstånd (AST). Bedömningen är ett mått på de samlade **symtombilderna** både **specifika** (t ex. nedsatt förmåga för social interaktion, kommunikation, stereotyper/ ritualer/ special intressen) OCH **koexisterande** (t ex. hyperaktivitet, tvång, depression, aggression).

Bedömningen av svårighetsgraden (S) utgår från den specificerade tidpunkten och bedömningen av förändring/förbättring (I) i jämförelse med en tidigare global uppskattning.

Namn:_____ Datum:_____

Specificerad tidsperiod: 1 månad

Ändring/förbättring (OSU Aut CGI-S)

Välj lämplig kodning:

☐ 1. **Inga** symtom på AST.

☐ 2. **Svaga** tecken på AST, men symtomen är subtila. Omgivningen lägger inte märke till att personen har svårigheter inom AST.

☐ 3. **Mild** AST, märkbar symtombild men generellt sett har personen fortfarande ett adekvat fungerande i vardagen.

☐ 4 **Medelsvår** AST, klara svårigheter inom autismspektrum. Personen behöver stöd och hjälp i vissa vardagssituationer.

☐ 5 **Måttlig till svår** AST, uppenbara svårigheter inom autismspektrum. Personen behöver stöd och hjälp i många situationer; från de enkla och vanliga till situationer där symtomen på bristande delaktighet i strukturerade aktiviteter och vardagssituationerna behöver förebyggas.

☐ 6 **Svår AST,** symtomen är betydligt svårare. Personen är i behov av permanent stöd, vård och omsorg pga. följande symptom t.ex. begränsningar, självskadebeteende eller aggressivt beteende mot omgivningen.

☐ 7 **Extrem AST,** symtomen är genomgående svåra. Personen är i behov av institutionsvård, ofta åtföljande symtom (t.ex. omfattande begränsningar, självskadebeteende eller aggressivt beteende mot omgivningen), som hotar personen säkerhet och/eller omgivningen potentiellt.

Alane Kadouri, Emmanuelle Corruble et. al, The improved Clinical Global Impression Scale (iCGI): development and validation in depression, BMC Psychiatry 2007. Svensk version: Nora Choque- Olsson & Sven Bölte, 2011.